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## ARGUMENT ON NEURAL TUMOURS AND THEIR ALLIES

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### INTRODUCTION

this series is presented mainly in argument, it need not be rigorously evant or detailed. Actually it represents one example of the usefulness for discussion of various subjects included in a larger projected work called "The Cancer Registry," in which I deal, for collection in this Laboratory of over 25,000 indexed tumours, with subject of tumours in general. The method adopted in this argument is to confine it to reflective discussion on each of the 27 variations separately. It would, of course, require a great many figures to deal adequately with the subjects illustrated and that, to present, is not possible. The figures given, however, present a table text for remarks on the histogenesis and histopoiesis of some tumours and some tumour-like lesions. I have placed considerable emphasis on an embryological approach, believing that to be the most rational for oncology in general. Historically I should say this method of approach was suggested by Virchow<sup>1</sup>; systematically presented by Cohnheim<sup>2</sup> with his "abgesprengte" or "abgeschnürte Keime"; elaborated by Albrecht<sup>3</sup> in his introduction of the terms "hamartias" and "choristas" with their respective lesions (-omas and -blastomas) and brought to a nearer and more reasonably normal focus by Compecher,<sup>4</sup> who introduced the idea of the ordinary, replacement, basal cell, for epithelial tumours at least, in the term "Basalioma."

New growth, as true tumour growth, is difficult to define. The latest example of new growth, though not tumour, is the progressive and regressive development of man through the eight stages of his existence: egg, embryo, foetus, infant, child, adolescent, adult and senescent. These are, very roughly, stages of growth which total one even two more than those of Sir Thomas Browne<sup>5</sup> and more than seven ages of Shakespeare.<sup>6</sup>

<sup>1</sup> 1803, p. 3.

<sup>2</sup> 1875, p. 68 and 1877, pp. 622-691: "Verlagerung," dislocation; "Versprengung," dispersal; "Verwirrung," disorder.

<sup>3</sup> 1904, p. 153.

<sup>4</sup> 1903, Intro., p. v.

<sup>5</sup> 1645, p. 84.

<sup>6</sup> *As you like it*, Jaques.



A fairly recent turn to the conception of progressive growth, accompanied by tissue or organ differentiation, is that presented in modern experimental embryology which embodies the abstract notions of organiser action, determination, segregation, induction, evocation and individuation. Differentiation and grading are the key note of this scheme of growth. It may be well to assert now that there seems to me little evidence either in normal or abnormal growth to support the contention of "dedifferentiation" or return from an actually differentiated to a less differentiated state. "Anaplasia," a term introduced and defined by v. Hansemann,<sup>7</sup> with the etymology ἀνά back (zurück) and πλάσσειν to mould, was applied to tumour growth with this very positive connotation and with express exclusion of even any suggestion that the return was to an embryological condition. It is, however, this very embryological condition of the basal, immature, or stem tumour cells which I shall endeavour to uphold. The term anaplasia was in fact taken by many workers to mean this embryonic condition and elicited a protest from v. Hansemann<sup>7</sup> (1909) under the title: "Was ist Anaplasie?" It seems to me that the etymology of the word, built upon a very rare use of the prefix ἀνά was at fault and has caused all the confusion. Moreover, there is no dedifferentiation, no reversion in anaplasia although there is non-differentiation, or if that is preferable a decrease in differentiation. The term is a misnomer and, even if well understood, should be abandoned. The growth of embryo, of tissue primordium, of cells and of tumour respectively should always be upward (Anabasis) and forward (Proso-plasia) and is not downward and backward. It is orderly and rapid in the embryo and foetus, each stage up to the adult representing a base depot of tissue for the development or determination immediately ahead. Tumour growth and indeed all growth is referable fundamentally and basally to embryonic cell growth and this seems almost to have been accepted for tumours of the nervous system if the classification of these tumours introduced by Bailey and Cushing,<sup>8</sup> or some modification of it remains acceptable. Physiological growth and neoplastic growth are essentially similar, while "malignancy" (Mallory<sup>9</sup>) is in some measure merely a matter of rate of growth with all that that entails in cells and tissue. The proliferative growth and activity of the differentiated cell is at an end, finished.

### NERVOUS SYSTEM EMBRYO

FIG. 1.—*Embryo*.—Pig, 6 mm. Showing in transverse section at the top the medullary tube and on either side derivatives of the neural crest—the primordia of the sympathetic ganglia and adrenal medulla. Lateral to these, more superficial and still at the upper end, are condensations to become better defined as somites. In the ventrolateral portion of the section the neural element should be represented by the primordia of the ganglia of the autonomic nervous system and the medulla of the adrenal in what I call the neuro-urogenital region. This is the region of the coelomic urogenital fold and is situated between intestinal mesentery and somatopleure. The most striking objects occupying

<sup>7</sup> 1890, p. 321 and 1909, p. 185

<sup>8</sup> p. 53.

<sup>9</sup> p. 268.

these folds are the large mesonephroi. In addition we note the intestine attached, fore and aft, by anterior and posterior mesenteries. Below the medullary canal is the notochord and then the aorta and in the lowest part of the section the body stalk. Courtesy of Professor H. A. Harris, Anatomy Department, Cambridge University.

It is natural that I should begin, even though very inadequately illustrated, with the nervous system of the embryo. The early stages may be set out as neural plate, neural groove, neural tube and neural crest. It has always seemed to me that the neural crest and its derivatives require more study. The crest tissue is a little indefinite, a bilateral club-shaped small mass between the neural tube and the epidermis, in close proximity to and destined to be metamerically segmented like the somite. If this close proximity is closer than is usually noted we might speak of the neuro-somite region as one of potential future tumour or tumour-like lesions (the *nævus*, neuro-fibromata and melanomata) and even adopt tentatively the name mesectoderm suggested for the early neural crest by Stone.<sup>10</sup> The somatopleure (Sm.p. Text-fig. 1), or early body wall of the intra-embryonic coelom, consists of a covering of a single-cell layer of ectoderm (periderm) and a thin layer of parietal mesoderm. The muscles, nerves and skeletal elements grow out into it (Hamilton, Boyd and Mossman<sup>11</sup>). Another region of great importance in oncology, one which might be called a meeting place of malformations and their allies the tumours, is the neuro-urogenital region of the coelom as I, perhaps rashly, call it. It is the region of development of the adrenal medulla and autonomic nerve ganglionic chain in close proximity to the urogenital ridge comprising the Wolffian (mesonephric) and Müllerian (paramesonephric) ducts, gonad and embryonic kidney (the mesonephros). Neurologically the adrenal medulla and the autonomic nervous system are important in the present discussion of some tumours of the nervous system, especially of the neuroblastoma, phæochromocytoma, ganglioneuroma and melanoma.

The neuromedullary tube in the plate-Fig. 1 is in the stage of a central canal surrounded solely by multilayered, uniform, undifferentiated cells, the indifferent cells of Schaper<sup>12</sup> which I may, if it does not violate accepted priorities, call medulloblasts or, perhaps better, neurogonia. There does not appear to be much differentiation yet from simple medulla cells to definitive nerve cells, glia cells, axones or neurofibrils, and the lining of the canal is wholly cellular without separation yet into its ependymal, mantle and marginal layers. The medulloblast, as one may reasonably call it, should give rise to a tumour of undifferentiated cell type, the medulloblastoma. One of the earliest differentiations of this "indifferent" cell or neurogonium is to the epithelial lining ependyma of the central canal and, headwards, of the ventricles and optic vesicles. The ependymal cell, again, has its tumour representatives in the ependymoma, the neuroepithelioma

<sup>10</sup> 1929, p. 40.

<sup>11</sup> 1945, pp. 44, 45, 318 and figs. 79, 170.

<sup>12</sup> 1897, pp. 84, 85.

and the medulloepithelioma. The intrusion of vascular, mesodermic meningeal tissue as choroid plexus gives us the subvariety of the ependymoma the choroidal papilloma, as it has been called by Kernohan and Fletcher-Kernohan<sup>13</sup> and Globus.<sup>14</sup> The extension laterally and outwards of the optical apparatus is an extension of the ventricular canal and provides tumours such as the neuroepithelioma (*Glioma retinae*) of the eye, or in a less determined stage, the retinoblastoma (neuroblastoma). In this last large cellular group neuropathologists include the medulloblastoma of the cerebellum, the neuroblastoma of the adrenal and, more debatably, the carcinoids of the gut and retroperitoneal tissue.

The meninx, derivative either of the neural crest or the mesoderm, supplies one main tumour, benign or malignant, with according to Bailey and Bucy<sup>15</sup> nine varieties: the meningioma.

#### PIGMENTED SHEATHS EMBRYO. NEURO-UROGENITAL REGION

FIG. 2.—*Tadpole*.—Transverse section, showing eye and neural tube in process of development. Pigmented sheaths are represented as lining the medullary tube; as the retinal pigment layer and subscleral lamina fusca; as cutaneous and pericœlomic pigment. Perivascular pigment sheaths are manifest, microscopically, around the smaller blood vessels. 13/39. I.A.P.

Pigment is more widely and differently distributed in chromatophore cells (melano-, erythro- and xanthophores) throughout the body in the lower than in the higher vertebrates and often even more in the larval than the adult forms. One may speak, for example, with Ehrmann<sup>16</sup> of originally pigmented and originally non-pigmented amphibian ova or with Weidenreich<sup>17</sup> of pigmented sheaths and their importance in the phylogeny and ontogeny of vertebrates. There is a primary pigmentation and a secondary pigmentation with intervening depigmentation to be considered. These sheaths (secondary pigmentation) are of some importance, even as vestigial manifestations, in man; for example the mongolian spot, the blue nævus and the melanosis (Virchow<sup>18</sup>) of the pia-arachnoid, because they have a distinct bearing on the discussion as to the real nature of the melanomata—epidermal, dermal, neural or mixed.

The amphibian embryonic pigment sheaths in the tadpole are illustrated in composite Text-figure 1 and Plate-figure 2 as cutaneous (dermic and epidermic), perimedullary, pericœlomic, perivascular retinal and choroidal, as well as in some other situations. The melanin of chromatophores, *e.g.* in frogs, fish and lizards enables them to change their cutaneous colouration in consonance with their environment under neural, neurocrine, or neurohumoral stimulus (Parker<sup>19</sup>; Hogben<sup>20, 21</sup>) by withdrawal centrally of the melanin granules from their arborescent cytoplasmic processes. In the slug (*Arion ater*), representative of the

<sup>13</sup> 1937, p. 186.

<sup>14</sup> 1937, p. 208.

<sup>15</sup> p. 15 *et seq.*

<sup>16</sup> 1896, p. 2.

<sup>17</sup> 1912, p. 80.

<sup>18</sup> 1859, p. 180.

<sup>19</sup> 1932.

<sup>20, 21</sup> 1922 to 1945.

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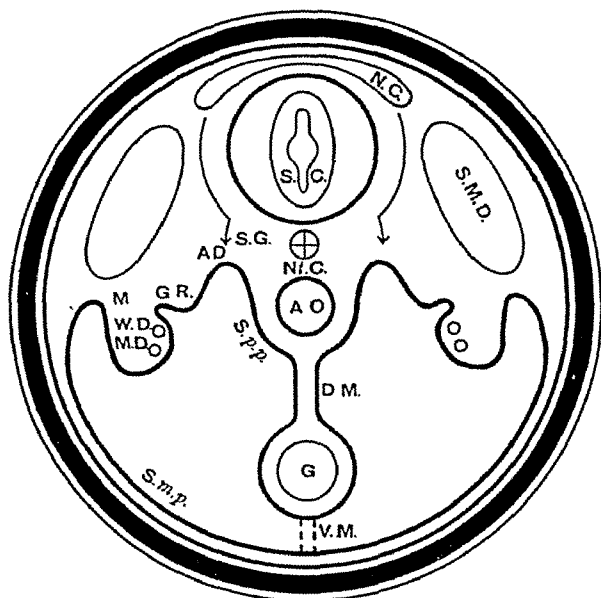
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non-vertebrates, illustrated by Harvey, Dawson and Innes <sup>22</sup> (Fig. 76, Melanoma), the melanin which gives it its notable blackness is very largely situated in subepidermic corium. These melanotic chromatophores are not phagocytic (fixed, or wandering) but true melanin-producing, melanin-containing cells—perhaps, cells *sui generis*. Their melanin granules are, in good preparations, of extremely uniform size—cytoplasmic granules (Wolff <sup>23</sup>).



TEXT-FIG. 1.—Transverse section. (1) Body of lower vertebrate embryo, to show epidermal, dermal, perineural, pericœlomic and perivascular pigment sheaths (after Weidenreich) : (2) Body of higher vertebrate embryo, to show the neuro-urogenital region of the cœlom. Pigment sheaths in deep black line and arrow from neural crest to sympathetic ganglionic chain and adrenal medulla.

AD., Adrenal. AO., Aorta. D.M., Dorsal mesentery. G., Gut. G.R., Genital ridge. M., Mesonephros. M.D., Müllerian (paramesonephric) duct. N.C., Neural crest. Nt.C., Notochord. S.C., Spinal cord. S.G., Sympathetic ganglion. S.M.D., Scleromyodermotome region. Sm.p., Somatopleure. Sp.p., Splanchnopleure. V.M., Ventral mesentery (disappears). W.D., Wolffian (mesonephric) duct. M-G.R.-AD., Neuro-urogenital region.

Much has been written about melanin and its primary connection either with cells of the epidermis, with cells of the corium and choroid, or with nerve cells, nerve terminals, and telodendrions. It would seem probable that in man, except for blue nævi (Fig. 4), mongolian spots, progressive melanosis (Bettley <sup>24</sup>), melanotic meninges (Virchow <sup>18</sup>), chromatophores of iris or choroid (Mann <sup>25</sup>; Wolff <sup>26</sup>), melanin in the course of evolution has become concentrated in basal epithelial cells of the epidermis. The oxydase which converts the premelanotic chromogen to a melanin is present in many vertebrates in a variety of cells, but especially in the mesodermic chromatophores. The melanoma, as an essentially melanotic tumour is claimed by

<sup>22</sup> 1940. <sup>23</sup> Personal demonstration. <sup>24</sup> 1938 and 1947. <sup>25</sup> 1928. <sup>26</sup> 1944.

various workers' to be, from their several view points, epidermal, neural, or mesodermal in character. It seems possible, arising out of this diversity of opinion, that melanin pigment has been over-emphasised as a chief, instead of an incidental, characteristic to constitute a specific tumour. The pigmented epithelioma, however, as a tumour distinct from the melanoma, was suggested by Johnston.<sup>27</sup> Various epidermic tumours (Becker<sup>28</sup>) may form melanin. The reaction, in general terms, which gives rise to melanin is set out by Lison<sup>29</sup> according to G. Bertrand as :

Ferment+acceptor+oxygen  $\rightarrow$  melanin.

According to Bloch<sup>30</sup> the ferment is a specific oxydase and the acceptor dihydroxyphenylalanin ("dopa"), an amino-acid allied to, or derived from, tyrosin. Bloch apparently makes all primary pigmented cells of the skin in man epithelial, excepting those of the mongolian spot. Melanoblasts are said by the neural school to have origin in the embryo from the neural crest and to migrate thence to the skin, nervous system and other parts to form the pigment sheaths of Weidenreich (du Shane<sup>31</sup>). The melanin of the epidermis is contained not only in basal epithelium but also in the cells, if they really be cells, described by Langerhans.<sup>32</sup> These latter are said to be neural—nerve terminals—with pigment-laden telodendrions reaching upwards from the epidermal base into the *stratum malpighii*. Melanin in general terms may be regarded, phylogenetically, as protective and labile where change of colour with environment is necessary; as static camouflage in hair-covered animals (*c.g.* tiger, leopard) and as protective barrier to actinic rays in the highest, hairless, animal man.

### THE BLUE NÆVUS

FIG. 3.—*Blue nævus*.—Low power, with high power magnification inset. Showing epidermis above of uninterrupted regular pattern at the corio-epidermal junction and little sign of excessive basal epithelial pigmentation. A deeply pigmented condition of the corium, greatest at a depth far removed from the epidermis, is evident in cells which are elongated and arranged in parallel, not perpendicularly, to the epidermis. This pigmentation, at sight, is of connective tissue only and not of epithelial cell elements; mesodermic, not epidermic, and probably of a specific cell element. 8970/46.

The name "blue nævus" itself challenges comparison with the "nævus cell" mole. Neither of them is a tumour; they are, following Albrecht,<sup>3</sup> "hamartias," although they may show as "hamartomas." Both of these congenital malformations may, however, develop into "hamartoblastomas" (true tumours), in which case they might, if malignant, be of the opposite types:—carcinomas or sarcomas. The carcinoma type is so much more common than the sarcoma that it is in practice the only one usually considered. There remains, however, a dispute which enrols many authors and is mostly concentrated on the benign nævus-cell lesion or mole: it fluctuates between views

<sup>27</sup> 1905, pp. 1 and 49.

<sup>30</sup> 1929, p. 618.

<sup>28</sup> 1946, p. 4.

<sup>31</sup> 1943, p. 109.

<sup>29</sup> 1936, p. 156.

<sup>32</sup> 1868, p. 325.

that its origin is to be found solely in the embryonic, somatic ectoderm (*e.g.* "abgeschnürt" Unna<sup>33</sup>; Dawson<sup>34</sup>); that it is, as tumour, of mesodermic chromatophore, not nævus-cell, origin (*e.g.* Ribbert<sup>35</sup>) and that it is neuroectodermic, a revival of the suggestion of Soldan<sup>36</sup> by Masson<sup>37</sup> (in several publications, *e.g.* 1926). Ribbert<sup>35</sup> has been the great proponent of the opinion that the nævus cell is genetically the mesodermic chromatophore itself, not epidermal and that its tumour representative should be "chromatophoroma." The condition illustrated here of blue nævus is blue for the same reason that eyes are blue: if the iris stroma is lacking in mesodermic chromatophores, the melanin pigment on the deep posterior epithelial surface of the iris appears blue: if, as in the albino, the epithelial melanin of the posterior surface is also absent we get the vascular pink eye. So it is with melanin pigment in chromatophores and epithelium of the tegumentary corium and epidermis. The blue nævus is closely related to such conditions as the mongolian spot, the slate-blue colouration of some monkeys and of the mouse, and with "progressive melanosis" (Darier<sup>38</sup>; Bettley<sup>39</sup>). In man it is essentially a chromatophore vestige. One may go further still and suppose that the blue nævus is representative of the cutaneous (dermal-epidermal) outer, mammalian and avian pigment sheath, one of the four (perimedullary, pericœlomic, perivascular and cutaneous) pigmented sheaths, according to Weidenreich,<sup>17</sup> of the amphibian and other lower vertebrate embryos. He derives all four sheaths from the ectodermic neurogenic plate: in the case of human melanotic chromatophores one might extend this to say, from the neural crest (Hamilton, Boyd and Mossman<sup>41</sup> and du Shane<sup>31</sup>). Although this conception of the chromatophore proper would derive all these secondarily pigmented cells from a neurogenic primordium, it is still possible to relate the pigmented chromatophore to the mesenchyme: it is represented normally in the human being in cells of the corium (some negro skins), the choroid, the anterior stromal tissue of the iris, the basal meninx in the region of the medulla oblongata and the perianal skin. We may indeed ask ourselves what is the chromatophore, the large pigmented cell with many cytoplasmic processes, exhibiting contractility of its very uniform pigment granules? According to Parker<sup>19</sup> in agreement with Weidenreich<sup>17</sup> and others, it is a cell *sui generis*, powerfully under hormonal and nervous influence,<sup>17</sup> as exhibited experimentally in, for example, the killifish (*Fundulus heteroclitus*<sup>19</sup>). Spaeth,<sup>40</sup> however, considers that it is a disguised muscle cell. I would also subscribe to the specificity of the cell and by linking it up with the pronouncements on the nature of the nævus-cell tumour—those for instance of Unna<sup>41</sup> from epidermis, Ribbert<sup>35</sup> (chromatophoroma) and Masson<sup>42</sup> with his Schwannian

<sup>33</sup> 1894, p. 746.

<sup>34</sup> 1925.

<sup>35</sup> 1914, pp. 318-362.

<sup>36</sup> 1890, p. 261.

<sup>37</sup> pp. 417-452 and 657-694.

<sup>38</sup> 1928, p. 957.

<sup>39</sup> 1938, p. 181 and *Proc. Roy. Soc. Med.*, 1947, p. 505, and 22, fig. 58, *Debatable Tumours, Melanoma*, p. 30. <sup>40</sup> 1916, p. 193. <sup>41</sup> 1893, pp. 14-16. <sup>42</sup> 1932, p. 367.



hypothesis relating the cells to sheath cells and to sensory nerve terminals of Merkel-Ranvier and Wagner-Meissner type in the skin—might tentatively suggest a denomination for the cell of “myoneuroglial.” Its smooth-muscle cell affinity is based largely on the contractility of the cell and the close resemblance to one another of neuroglial, myoglia and fibroglial fibrils. Its neural characterisation, even with designation attached of “mesenchymal,” may be given as due to its origin from the neural crest; again it might appeal to supporters of an epithelial theory as “myo-epithelium,” or as a “myo-neurone.” As chromatophore it can be a cell connected through its dendrites to a neuraxon plexus and by other dendrites to melanotic telodendria reaching up between and into epidermal cells, the so-called Langerhans’<sup>32</sup> cells. It may be related to the hair sheaths of short-hair bulbs which are, even more than the corpuscles of pain and touch, under the influence of a neural plexus (Lovatt Evans<sup>33</sup>). The benign melano-epithelioma was, indeed, declared by Acton<sup>41</sup> dealing with the melanoma from a comparative histology and phylogeny standpoint to be a suppressed hair field or hair area. The dendritic character of the chromatophore is very like that of the protoplasmic or fibrillary astrocyte, while the laminated sheath of many tactile corpuscles reminds one of the piloid astrocyte. In the genealogy of the several neuroglia cell types one might, with Masson (*loc. cit.*) link the chromatophore cell and its surroundings to nerve terminals; to the neurilemma cell of Schwann and its neuraxons; to the satellite cells around a ganglion cell, and in the central nervous system to the oligodendroglia. Thus we attach to the chromatophore cell various ectodermic and mesodermic affinities, mainly neurogenic; motor, sensory, autonomic; and have noted its separation as a cell *sui generis*; myo-epithelium, myo-neuroglia, myo-neurone, peripheral cell of the autonomic nervous system, basal epithelium and cell of the short-hair sheath or bulb—a very mixed sibship, which is probably near the truth and which may be excuse for the great variety of confusing opinions I have quoted. The melano-carcinoma is an epithelial tumour and it may be contended that the name melanoma is too much of a concentration on an incidental, though striking and diagnostic appearance—the presence of melanin. The carcinomas of *Xeroderma pigmentosum* are associated with congenital (naevoid) lack of melanin.

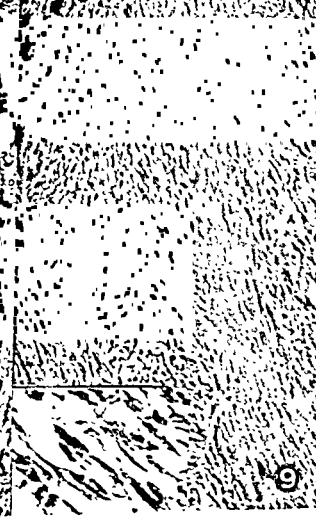
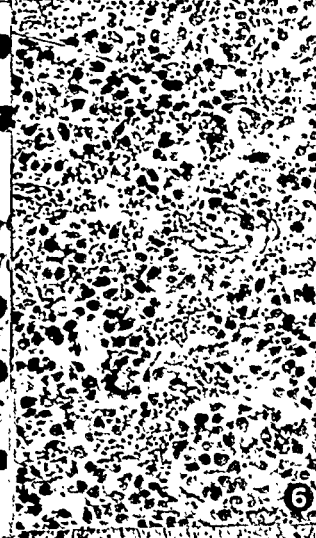
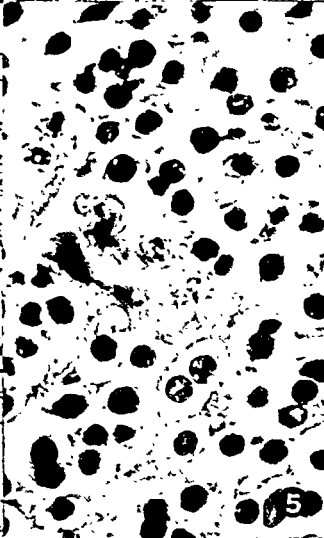
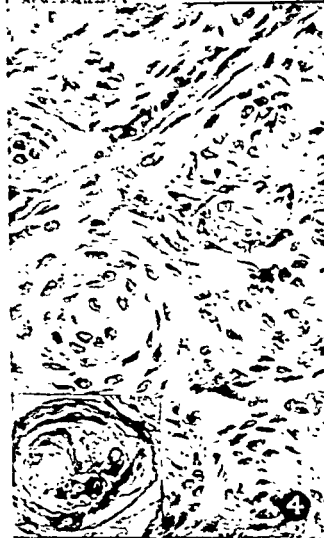
### MENINGIOMA

FIG. 4.—*Meningioma*.—Low power with high power whorl inset. Showing the typical leptomeningioma made up of very uniform tumour cells, forming many onion-like laminated whorls; no mitoses. The whorls have little or no intercellular stroma and the centre is without lumen, but may contain one or more loose flat cells. A whorl may become homogenized and may be calcified, when it is a psammoma body or calcospherite. 5271/38 and 4972/38.

It is the whorl of the meningioma which gives rise to the most difficulty in explanation. It somewhat resembles the “pearl” or

<sup>33</sup> 1945, p. 459.

<sup>41</sup> 1921 (antedated to 1911, W.F.H.), p. 493.





"cell nest" of the epithelioma and was at one time even identified with it. The ordinary cells of the tumour are the cells of the meninges and have been compared with those of arachnoidal granulations but this statement only translates the debate to one on the origin of these structures. If the centre of the whorl were a definite blood vessel lined by littoral endothelium there would be every reason to call the meningioma an angioendothelioma, more endothelial than angiopoietic and thus justify its original name of dural endothelioma. It is, however, very difficult to detect a vessel at the centre of any whorl. Much more commonly, if there is any centre to the whorl, it is a single cell with nucleus or sometimes a group of as many as three cells. This does not exclude the possibility that the whorl is a proliferation of cells around a blood vessel becoming laminated, for we may surmise that the lumen can be occupied by desquamated intimal endothelium. One would naturally argue that, even so, all the existent vessels should not contain only detached cells centrally but that some should remain patent. Debate arises also whether the meningiomas are neural tumours, *i.e.* whether they are neuro-ectodermic or mesodermic or, according to Stone,<sup>10</sup> both ("mesectodermic"). One argument which is greatly used in support of the neural origin is that Harvey and Burr,<sup>45</sup> from their experiments on embryos, deduced an origin for the leptomeninges from the neural crest. That argument does not yet seem to be wholly accepted and is not supported by the work of Weed<sup>46</sup> and Flexner.<sup>47</sup> The French school represented by Roussy and Cornil<sup>48</sup> adhere to a neuroglial origin and extend this to the neurilemma sheath. Mallory<sup>49</sup> and Penfield<sup>50</sup> pronounced emphatically for a fibroblastic character and make the meningeal covering of the cord and brain the homologue of the covering (epi-, peri- and endoneurium) of the cranial and spinal nerves. By using the term "meningioma" for the tumour Cushing<sup>51</sup> confessed his inability to decide dogmatically on this point and so that name gives no indication, generically or genetically, of the histogenesis of the tumour except that it does arise from the meninges. The melanotic meningioma of Bailey and Bucy<sup>52</sup> takes us back in argument to Weidenreich's<sup>17</sup> pigment sheaths of the embryo and to Virchow's<sup>18</sup> diffuse melanosis of the arachnoid.

### OLIGODENDROGLIOMA

FIG. 5.—*Oligodendroglioma*.—Showing a field of tumour composed of very epithelioid cells which do not seem to have cell processes: these processes are, in any case, scanty ( $\delta\lambda\iota\gamma\omicron\varsigma$  few,  $\delta\epsilon\upsilon\delta\omicron\upsilon\mu$  tree). Nuclei are spherical with moderate chromatin and the cytoplasm is abundant. A solid alveolar, or pseudoalveolar, pattern, as in this illustration, is often a feature of this tumour. N.S., C.G., N. 199, H. 21, S. 21.

The oligodendroglioma in biopsy practice is a tumour of some rarity, but is striking in character when found. The original oligo-

<sup>45</sup> 1926.

<sup>46</sup> 1917.

<sup>47</sup> 1929, p. 35.

<sup>48</sup> 1925, pp. 75-78.

<sup>49</sup> 1920.

<sup>50</sup> 1923.

<sup>51</sup> 1922.

<sup>52</sup> 1931.

dendrocyte, to which category the tumour cells should belong, was described from this laboratory by Ford Robertson,<sup>53</sup> though under the name of "mesoglia." Other glial cells to which the oligodendrocyte has homologous affinity, or with which it is to be identified, are perineuronal satellite cells and the neurilemmal (Schwann) or neurinal (*ἰς, ἰνός* fibrous vessel) sheath cells of the peripheral nerves. Kernohan and Kernohan<sup>13</sup> rather surprisingly seemed to include the oligodendrogliomata with the ependymomata. In my own examples I have been struck by the resemblance of fields, selected as being specially diagnostic, to a pavement or parquet epithelium. There is little intervening, intercellular, fibrillar tissue, as Cox<sup>54</sup> points out, in these fields: the cells are large with considerable cytoplasm and the cell membrane appears not only to be thickened, as is often the case with juxtaposed cells, but to be cemented to the neighbour cell. The field chosen, may, however, be one of the pseudoalveolar fields described by Rio-Hortega.<sup>55</sup> If the supposition that the tumour is really ependymal is correct the epithelioid nature of the oligodendrocyte would contribute some support, but the argument would have to take into account suggestions not only of homologies with perineuronal satellite cells and neurilemma cells but also resemblances to astrocytes (Penfield<sup>56</sup>). The oligodendrocyte was fully described and named oligodendroglia by Rio-Hortega.<sup>57</sup>

### PINEOBLASTOMA

FIG. 6.—*Pineoblastoma*.—Showing large cells combined in no special pattern, but of uniform type. The conjunction of lymphocytes, or lymphocyte-like cells is very characteristic of this tumour. No distinction is drawn here between pineoblastoma and pinealoma. N.S., C.G., N. 200, H. 22, S. 22.

The pineoblastoma or, since this term as Cox<sup>54</sup> (p. 876) points out has been merged in medulloblastoma, simply pinealoma, is a curious tumour for a glioma. Morphologically it is often very characteristic in the conjunction of small lymphocyte-like cells with the parenchymatous tumour cells. These tumours are sometimes associated, though not necessarily, with *pubertas præcox* as in figure of Harvey, Dawson and Innes<sup>22</sup> (Granulosa-cell Tumours, Fig. 34; legend 14): it is ascribed (Russell<sup>58</sup> and others) to abnormal stimulation of the hypothalamus. The pineal body as "epiphysis" has not the status or importance in the human being of the "hypophysis." The pinealoma, first recognised by Krabbe<sup>59</sup> is described by Cox (p. 876) as apparently developing from medullary epithelium. In other words the pinealoma would be a glioma with differentiations to ependyma or glioblast (Cox, p. 877). Teratomas or teratoid tumours are met with in the region of the pineal body and many of the so-called "pinealomas" are probably of this nature (Russell<sup>60</sup>).

<sup>53</sup> 1899 and 1900.

<sup>54</sup> 1933, p. 868.

<sup>55</sup> 1934, fig. 43, p. 63.

<sup>56</sup> 1938.

<sup>57</sup> 1921.

<sup>58</sup> 1939, p. 162.

<sup>59</sup> 1916.

<sup>60</sup> 1944, p. 150.

## NEUROFIBROMA

FIG. 7.—*Neurinoma* (acoustic, cerebellopontine angle tumour).—Showing bundles of tumour cells travelling in different directions. The palisading of the nuclei is a special feature and, with higher magnification, the fibrillar prolongation of the cytoplasm, strikingly parallel between the arrays of nuclei would be manifest. 6357/35.

In this illustration of an acoustic neurinoma the most prominent feature is the palisade in which two opposing ranks of nuclei are separated by a parallel system of fibrils; these fibrils belong to and are a continuation of tumour cells. This phenomenon of fibrillar palisade, or what is a more frequent occurrence, one of fibrillar and nuclear arrangement in fasciculate echelon, is found in the spinal and peripheral nervous system as well as in the eighth cranial nerve tumour. The title heading given to the text is "Neurofibroma" because debate circulates around the contentions that the tumour is glio-, neuro-, or fibroblastic. Many, probably most, of the neurofibromata of the skin region, and notably in cases of Recklinghausen's multiple neurofibromatosis are, at least apparently, more fibromatous than neuromatous—*molluscum fibrosum*. The term neurinoma which is applied to the acoustic nerve tumour and was introduced by Verocay,<sup>61</sup> signifies that it has a truly sheathing fibre (ἰς, ἰνός, fibrous vessel, strength) composition, but that name as given, was intended to signify a neural not a collagenous fibre sheath. Much depends therefore on whether we allocate this fibre, so well shown in the palisade, to fibrogia or neurogia, to fibroblast or the peripheral glioblast of Schwann<sup>62</sup> (neurilemma cell). The neurilemma cell as seen in the internodal segments of peripheral nerves is cytologically a most interesting cell. It appears to have an abundant cytoplasm, to be multipolar and to have many bulky cytoplasmic processes of astrocyte type spreading in all directions over the surface of the myelin. If this, the neurilemma cell, is the true component cell of the neurofibroma we may, perhaps, be justified in regarding the palisade as a compression effect of protoplasmic processes which in this way become parallel and piloid. One might speculate still further and assume, on experience and on morphology grounds, that the glial cell, embryologically as polar spongioblast and in adult life as astrocyte, tends inevitably to be a multipolar type of cell. Then why should the question of fibroma enter upon the stage of discussion? Well, the nerve fibre is surrounded by endoneurium, a fibrous sheathing supporting stroma and neurilemma cells are difficult to distinguish as cells (Bailey and Hermann<sup>63</sup>) from fibroblasts, whatever may be the case for reticulin or collagen. A connecting link of neurofibromatosis with multiple melanomata is furnished by the characteristic pigmented skin areas (café-au-lait) first noted by v. Recklinghausen himself. A similar condition is noted also in the clinical complex with neural tumour background, known as Albright's syndrome.

<sup>61</sup> 1910, p. 65.<sup>62</sup> 1839, pp. 171, 2.

Figs. 6, 7. Tab. IV.

<sup>63</sup> 1938, p. 33.

## GLOMANGIOMA

FIG. 8.—*Glomangioma*, with inset a higher magnification of some "glomus" cells. One of several angiomatous tumours of the skin in a girl aged  $7\frac{1}{2}$  years is illustrated. Similar tumours were present in the father (familial). Showing blood vessels, discrete in the section field and surrounded by many layers of glomus cells. The vessel has its endothelial cell lining and the glomus cells occupy the position of the tunica media, but are not complete in some of the vessels. The high magnification gives, for the field chosen, a very epithelioid and pavement appearance to the cells, although for the most part there is a little intercellular matrix tissue separating them. 8915/33 and 8575/36.

A glomus cell has much physiological interest. Histologically the typical malformation, or tumour as the case may be, is comparatively easy to diagnose at sight. Thick-walled blood vessels are surrounded, more or less in the position of the tunica media of an artery, by closely set epithelioid cells. Clinically notice is drawn to the lesion, and this may suffice for direct diagnosis, by the symptom of excruciating pain and if, in addition, this is subungual in position it is simple to decide upon the "painful subcutaneous tubercle" of Wood.<sup>64</sup> Pain, however, is not always a symptom and the lesion or organ is by no means always or commonly, subungual. The interest of the condition centres, perhaps, more around the nature and function of the glomus or glomerulus as neuro-myo-arterial than on its pathology. We are familiar with the structures named *Glomus caroticum* and *Glomus coccygeum* but what is then their function? There are other glomera than these and the question may even be extended to glomeruli, say of the kidney or the intestinal villi. There are various suggestions to be considered: whether these are glands of internal secretion or paraganglia (Kohn<sup>65</sup>); whether even if admitted to be neural they are not primarily vaso-muscular; whether if neural they are chromaffin or non-chromaffin, adrenergic or cholinergic (Dale<sup>66</sup>). In fact what are the glomus cells, the large epithelioid cells of the glomus? It is generally accepted that one of the functions of glomera is the promotion of direct retro-venous blood flow from the artery by a specific connecting complex of blood vessels. This direct vessel, or these vessels, with the nerve plexus around them form the characteristic feature of the glomus and also the glomangioma. It is of short length and is surrounded especially at the transition sphincter, by a network of fine nerves. The glomus cells are not ordinary arterial muscle cells, being polyhedral and epithelioid, lacking cell fibrils and having a very evident limiting cell membrane in close juxtaposition to, but separated from, its neighbour cells by a little stainable matrix. As a shunt system, are the contraction and dilatation activities both effector activities (double innervation) or only one of them? If contraction is one of these activities it is likely to be an adrenalin phenomenon. Dilatation seems accepted in man as a parasympathetic activity which may be due to liberation of acetyl choline and there are those, particularly Schumacher,<sup>67</sup> who insist that the epithelioid glomus muscle cell is

<sup>64</sup> 1812.<sup>65</sup> 1903.<sup>66</sup> 1934, p. 838.<sup>67</sup> 1938, p. 127.

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cholinergic. Still more questions may be asked, if not answered, about these cells. Are glomus cells, like the muscles of the iris and sweat ducts, myo-epithelial, neuroepithelial, and is the function of the glomus protective against cold or a means of heat regulation? Is the muscle cell itself a nerve terminal? These are physiological questionings. There are several lesions of the arteriovenous anastomosis type, such as "cirroid aneurysm" and the blood vascular tumours of the brain (Cushing and Bailey<sup>68</sup>), which might be called glomangioma: they may possess especially the characteristic rich network of nerves although wanting in glomus cells. Vessel-dilating substances of the tissues and their dependence on nerves have been dealt with by Dale,<sup>66</sup> Gaddum,<sup>69</sup> and others in classical publications. The treatment of the shunt circulatory system and arteriovenous anastomosis also has outstanding authors, Sucquet,<sup>70</sup> Hoyer,<sup>71</sup> Grant.<sup>72</sup>

### NEUROGENIC SARCOMA

FIG. 9.—*Neurogenic sarcoma*.—Woman aged 23 years. Tumour occupying a considerable length of the lower part of the sciatic nerve. Amputation of limb. Inset: higher magnification with mitotic figure. Showing fasciculate pattern: polymorphism of cells which are mainly elongated and hyperchromatic. Monster cells and mitotic figures were present. 2516/31.

Much the same arguments apply to this tumour as to the neurofibroma. Is it a fibrosarcoma or a gliosarcoma, *i.e.* is it mesodermic or neuroectodermic; is it a product of fibroblasts or neurilemma cells? The staining reactions of the cells themselves provide little clue. Bailey and Hermann<sup>63</sup> came to regard the fibroblast as indistinguishable in this respect, cytoplasmically, from the neurilemma cell. Reliance has to be placed upon the products of the cell or matrix, collagen, reticulin, elastin and so on. Fibroglial, myoglia and neuroglial fibrils can be thrown into special prominence by appropriate stains. The question then still remains, is the neurogenic sarcoma a fibrosarcoma or a gliosarcoma? Possibly it may be either or even both. The neurilemma cell, one must concede is neural, *i.e.* glial and a derivative of the neural crest but embryogenetically and experimentally, the distinction at embryonic and foetal stages of tissue growth between the cell types and their earliest morphological differentiation is not as strict as is implied in the usual rigid subdivision into "germ layers," or "derms."

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<sup>68</sup> 1928.

<sup>69</sup> 1936.

<sup>70</sup> 1862.

<sup>71</sup> 1877.

<sup>72</sup> 1929-31.

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(To be continued)

# PSYCHOLOGICAL AND SOCIAL ASPECTS OF SYDENHAM'S CHOREA

By E. R. C. WALKER, B.A., M.D., F.R.C.P.E.

## I. INTRODUCTION

IN 1685 Thomas Sydenham gave an admirable clinical description of the disease to which his name is now attached. He ascribed it to a humour which, entering into the nerves, irritated them and caused the movements (Latham, 1850; Babonneix, 1937). The two hundred and sixty years that have passed since then have yielded much information and produced a voluminous literature concerning the disease, but it is no great exaggeration to say that even to-day we cannot be much more accurate in our definition of its pathogenesis. The questions that still remain unanswered are: (1) what is the nature of the "humour"? (2) what produces it? and (3) how does it act to produce the resultant movements? The answers given to these questions at any period during the past two hundred years commonly reflect the prevailing medical bias of their time and the country of origin. A good deal was written in the eighteenth century to which reference was made in a monograph by Bernt of Prague in 1810. In the same year Bouteille in Paris published a treatise, and is said to have been the first writer to speak of rheumatical chorea, though the association was also noted by Bright in 1802, and Addison has been quoted as the first to draw attention to it. The great development of clinical hospital medicine of the nineteenth century finds expression in the many studies which began to appear during this period in France, Germany, America and notably in this country where the condition was particularly common—so common in fact that it was sometimes known on the Continent as chorea anglorum, though the appellation was mainly used for purposes of differentiation. The names of See and Roger in France, Romberg and Steiner in Germany, Weir Mitchell, Jacobi and Osler in America, and Fagge, Hughlings Jackson, Broadbent and Gowers in this country are among many associated with this stage. These studies established beyond doubt the close association of the condition with juvenile rheumatism. They were based on systematic clinical observation and pathological investigation. In the latter part of the century the birth and development of bacteriology opened a new approach and exerted a profound influence—an influence that may be said to have been dominant until quite recently. Bacteriological approach combined with the clinically proven association of chorea with rheumatism went far to crystallise ætiological opinion, so that, as Usher wrote in 1938, the causal relationship of the latter to the former "has grown almost into a tradition." Since about 1935, however, certain considerations have

caused an increasing number of workers, notably in North America (Gerstley, 1935; Coburn, 1937; Usher, 1938), but also in this country (Walker, 1935; Hubble, 1943), to challenge the validity of this tradition and to return to the more open-minded attitude of the pre- and early bacteriological era.

That chorea could be induced by purely psychological influences was held by many of the older writers. Broadbent (1869) wrote: ". . . I cannot but conclude that shock is not uncommonly the real cause of this affection," and looked upon "chorea in the child as, in some sort, the equivalent of insanity in the adult." According to von Ziemssen (1878), "Psychical disturbances, whether acting acutely in the form of fright or dread, or bringing to bear the slow depressing influences of sorrow and fear, of pain or discontent, are without doubt powerful agents in bringing the disease to an outbreak . . ." Risien Russell (1899) asks ". . . how are we to explain by this hypothesis (*i.e.* that chorea is infective in origin) those instances in which the manifestations of chorea have followed so closely on fright that it seems impossible to escape from the assumption that we are dealing with cause and effect?"

In his skilful analysis of "The Nature of the Rheumatic Child," Hubble (1943) expresses the view that the bacteriological researches of recent decades "have produced much knowledge but no finality." "The comparative failure of these researches," he considers, "demonstrates the need for returning to the pre-occupations of sixty years ago, to the study of the soil rather than of the seed, for it is here that the key to this 'peculiar type of host response' must eventually be found."

About fifteen years ago it began to be appreciated that the erythrocyte sedimentation rate was a valuable guide to the progress of rheumatic disease as well as of tuberculosis (Hill, 1932, *et al.*), and it became a routine practice in most children's hospitals to carry out E.S.R. tests at regular intervals in all children with rheumatic disease. It was soon discovered that in a number of children with chorea, but without either arthritis, carditis or nodules, the readings were more or less normal. Here seemed to be another difficulty added to the known apyrexia and normal leucocyte counts in these children, in the way of accepting an infective process as an essential ætiological factor.

Might it be that chorea was in fact what to simple observation it appeared to be, namely, an exaggerated fidgetiness resulting from prolonged apprehension and embarrassment, and that the frequent rheumatic concomitants were in casual and not causal relationship to it?

It is surprising to find in the copious literature on this disease, one in which there is obviously a great disturbance of the emotions, so little record of attempts to investigate factors which might be expected to lead to such disturbance.

To make a contribution to the study of such factors was the object of the investigation here described.

## 2. NATURE OF INVESTIGATION

It was decided to make an attempt to study the soil in which chorea developed. For this purpose the mother (and sometimes also the father) or guardian of each child treated for chorea in the principal medical ward of the Royal Aberdeen Hospital for Sick Children, or

## PRO-FORMA

## C H O R E A

Name :

Age :

Address :

Case No. :

1. Number in Family :

2. Position in Family :

3. Age of nearest sibs., how much older or younger :

4. Character of Mother :

(a) Education—good, average or poor.

(b) Intelligence—good, average or poor.

(c) Emotional make-up :

Excitable, irritable, calm :

Conscientious, over-conscientious, careless :

Normally affectionate, over-affectionate, indifferent :

Domineering, normally firm, weak :

(d) Special Remarks :

5. Character of Father :

(a) Education—good, average or poor.

(b) Intelligence—good, average or poor.

(c) Emotional make-up :

Excitable, irritable, calm :

Conscientious, over-conscientious, careless :

Normally affectionate, over-affectionate, indifferent :

Domineering, normally firm, weak :

(d) Special Remarks :

6. Difficulties in Family :

7. Difficulties at School :

8. Other Psychological Difficulties :

9. Manifestations of Rheumatism :

10. Any Other Chronic Infection :

in the out-patient department, was interviewed on one or more occasions. The object of the interview was to determine in addition to the usual history of birth, feeding, previous illness and family history, the presence of any factors which might adversely affect the child's mental and emotional stability. The above pro-forma was used to guide the investigation and explains the type of information that was sought.



It was felt that such adverse factors were most likely to be found in the circumstances of the home or of the school. In this connection it is interesting to note that while most authors refer to the possible ætiological influence of school life, comparatively little has been said of the part played by home circumstances. It is indeed hardly surprising that school life should have attracted attention in the ætiological study of a disease of which the incidence is over 80 per cent. in the normal school age.

An attempt was made to estimate the mental and emotional attributes and make-up of the parents. Relations with other children in the family, with other relatives and with neighbours were enquired into and an endeavour made to assess the physical and economic conditions of the home. Once the object of the enquiry had been explained, most of the mothers were readily co-operative: sometimes so enthusiastically so that their contributed information had to be accepted with a certain reserve. Information regarding school life possibly suffered in accuracy by being obtained at second-hand through the parents, but in a number of cases the parents had already discussed the situation of the child with the teacher, or did so after the first hospital interview.

Originally, 53 cases were studied. These represent for practical purposes an unselected series. During the years 1935 to 1939 inclusive, 72 cases diagnosed as chorea were treated in the hospital. In some of these cases it was not possible to arrange the necessary interview; and the whole enquiry had to be abandoned on 1st September 1939. It has been necessary to discard 7 cases on account of the incompleteness of the hospital records, and four others in which the diagnosis of chorea was not sustained (3 habit spasm, 1 hysteria). Forty-two cases, therefore remain and form the basis of this study.

### 3. GENERAL ANALYSIS OF THE SERIES

In general, analysed as regards the points usually studied in such series, such as sex, age of onset, season of onset, etc., the present series conforms to others investigated in this country.

(i) SEX.—Of the 42 children concerned, 27 were girls and 15 boys. Adding the 7 cases omitted on account of incomplete records, the figures would be 33 and 16, giving the usual ratio of rather more than two girls to one boy.

(ii) AGE AT ONSET.—The average age at onset of the first attack was almost exactly 8 years—in the case of the girls exactly 8 years and for the boys 8·1 years—though the greatest number of cases occurred at the age of nine. A curious feature appears on plotting graphs of the age of onset. A combined graph (Fig. I) of the whole group shows a fairly steady rise from the age of five to a peak at ages eight and nine and thereafter a steady fall. If, however, the sexes are separated both curves show a drop in the middle of the rise, in the case of the girls (Fig. III) at age seven and in that of the boys (Fig. II) at age

## PROTECTING YOUNG TEETH

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- (a) It is of obvious importance that the cleansing agents employed should be completely free of abrasive action.
- (b) Powerful astringents are contra-indicated, as these may irritate and inflame the gum membrane.
- (c) The essential oils incorporated must have a pleasant appeal to the young patient.

In all these respects, Phillips' Dental Magnesia presents a dentifrice which can, with confidence, be recommended to children of all ages. Completely free from harmful ingredients, it possesses a unique flavour which makes a very strong appeal to the young. Phillips' Dental Magnesia has, moreover, the outstanding property of inhibiting oral acidity by reason of the 'Milk of Magnesia' \* content, a very real advantage in protecting young teeth.

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Fig. 1



Fig. 2

# DEEP MALLEOLAR ULCER

## Healed with Standard Bandaging Technique

**Case History.**—G. J. Aged 45. Grocery Assistant. The patient first attended the clinic with a deep punched-out ulcer above the left internal malleolus . . . surrounding skin inflamed. (Fig. 1).

**Treatment.**—16th August 1946. Sulphanilamide powder was dusted into the ulcer, and calamine lotion applied to the inflamed area. An adhesive felt pressure pad was placed over the ulcer only, with a strip of Ichthopaste to cover the ulcer and the inflamed area. Elastoplast stirrups were applied and bandaging completed from toes upwards. (Fig. 2).

27th September 1946. The ulcer and the devitalised skin area completely healed. (Fig. 3). The patient was instructed to apply calamine lotion, pad of cotton-wool over the ulcer site, and to continue support with Elastocrepe for a few weeks.

Details and illustrations above are of an actual case. T. J. SMITH & NEPHEW, LTD., Manufacturers of Elastoplast, Elastocrepe and Ichthopaste, are privileged to publish this instance, typical of many, in which their products have been used with success, in the belief that such authentic records will be of general interest.



Fig. 3

# PRE-NATAL DIET

## and the course of PREGNANCY

The normal functioning of the reproductive organs during pregnancy depends, among other things, upon an intake of vitamins and minerals.

Medical opinion is gaining ground that an increased quantitative requirement for vitamin B is indicated in late pregnancy and the early puerperium. Its administration during the period before childbirth has resulted in less vomiting and nausea and in marked improvement in the nutritional value of the breast milk. In order to assure the building of the foetal bones *in utero* and a supply of a necessary constituent of the breast secretions, the importance of calcium is also established.

In Supavite Capsules the practitioner has at hand a combination of these and other essential vitamins and minerals in scientifically balanced form of particular value in maternity cases.

The value of the constituents of 'Supavite' in pregnancy may be summarised as follows:

### Vitamin A

Assists growth. Anti-infective and anti-xerophthalmic.

### Vitamin B<sub>1</sub>

Assists growth. Aids functions of the gastro-intestinal tract and the nervous system.

### Vitamin B<sub>2</sub>(G)

Maintains nervous stability, healthy skin. Assists digestion.

### Vitamin C

An adjuvant in lacteal secretions.

### Vitamin D

Maintains calcium-phosphorus balance in the blood. Mobilises bone-forming substances.

### Vitamin E

The fertility or anti-sterility vitamin.

### Iron

For correcting tendency to anaemia.

### Calcium

An aid to formation of foetal skeleton and enrichment of breast milk.

### Phosphorus

Necessary in general metabolism and the nutrition of the nervous system.

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CAPSULES

THE ANGIER CHEMICAL CO. LTD. 86 CLERKENWELL RD. LONDON, E.C.1

of eight. Though with such small numbers this feature may well be without significance, it is nevertheless interesting to note that the form of the curves is strikingly similar.

This age-incidence corresponds with that found by Walker (1935), who also found a secondary peak about puberty, but it differs to some extent from that given by Wilson (1940) who, in discussing "the period of maximum liability," states that "from details concerning individual years that of puberty (13) is found to stand out, but in Fletcher's series of 600 cases (at Guy's Hospital) it was the tenth

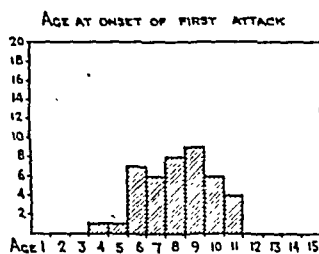


Fig. I.

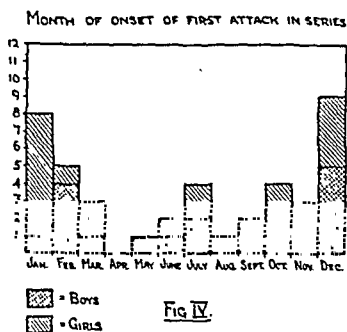


Fig. IV.

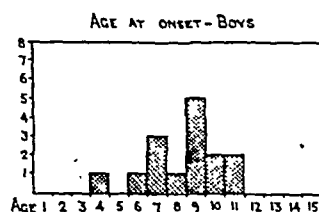


Fig. II.

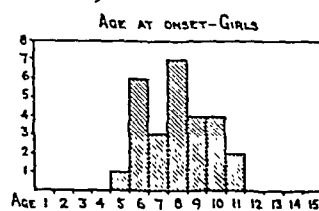


Fig. III.

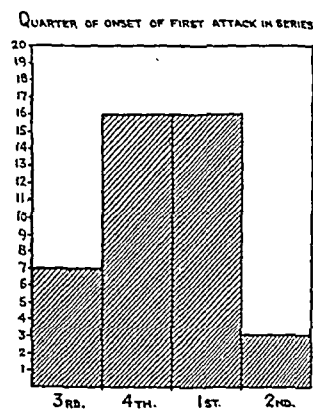


Fig. V.

year." In neither case is it made quite clear whether the figures refer to the age at onset of the *first* attack.

The age-incidence in America seems to be higher than that recorded in the present series. Hedley (1940) in a series of 687 cases of all ages in Philadelphia gives the mean age as 10.5 and the median age as 10.1, "based on the age of the patient during the initial admission in the period under study." Hempelmann (1925) places the greatest incidence "between the seventh and thirteenth years."

Since the present series deals only with children up to the age of twelve (the maximum age for admission to the hospital) and thus misses the "puberty" cases, it is probable that the age-incidence

agrees closely with that normally found. Out of the 42 children concerned, 36 began their first attack between the ages of six and ten.

(iii) SEASON OF ONSET.—Fig. IV shows the month of onset of the 42 first attacks. Seventeen (40 per cent.) of these occurred in December or January, and 32 (76 per cent.) between October and March. This winter preponderance is in line with the usual British experience. Wilson (1940) quotes Fletcher as finding "peak" months in December and January in 574 cases recorded in the St Bartholomew's Hospital Reports (1896). American experience on this point is more varied than the British, so that whereas Lewis in a collection of 1387 cases in Boston and Philadelphia found that by far the greatest number occurred in March, April and May, Abt and Levinson in Chicago reported that season did not play a constant rôle in their series of 226 cases (Abt, 1925; Wilson, 1940). Hedley (1940), taking *the month of initial admission to hospital* in 687 cases in Philadelphia, found a slight preponderance in the first half of the year (57·7 per cent.), and only 16·6 per cent. in the last quarter.

(iv) ASSOCIATED RHEUMATISM.—Under the heading Rheumatism were included carditis, arthritis, nodules and growing pains. Where doubt existed, a positive finding was recorded. A history of tonsillitis was not regarded as evidence of previous rheumatism. If it were, then at least half the juvenile population of the North-East of Scotland would have to be considered as having suffered at one time or another from rheumatism.

A. *Previous Rheumatism*.—Fifteen (36 per cent.) of the 42 children gave a positive history of illness which could be regarded as rheumatism, 10 girls and 5 boys. Four others, 2 girls and 2 boys, had a history of chorea without other evidence of rheumatism (what has been called in America "pure" or "straight" chorea), making 19 (45 per cent.) in all with a possible history of previous rheumatism.

B. *Concurrent Rheumatism*.—In 17 of the children, 13 girls and 4 boys, a rheumatic lesion was either present or suspected (in all cases carditis) during the period of hospitalisation. In only one case (No. 25) were nodules noted, and she also probably had a carditis. She had an E.S.R. of 20. Her subsequent history is encouraging. She had no recurrence of chorea, remained well, married and has a baby. In no case was concurrent arthritis observed. In 6 of these 17 cases the diagnosis of carditis was doubtful. In 2 the E.S.R. was normal, and all 6 subsequently remained well and without recurrence of chorea. Two, however, had had sore throats with fever within a month of admission.

Somewhere between 25 and 40 per cent. of the series may be considered to have had concurrent rheumatic lesions. In 16 of the series the E.S.R. was not found at any time during the period of observation to exceed 12 mm. in one hour.

C. *Subsequent Rheumatism*.—It has been possible to follow up 34 of the series, 24 girls and 10 boys. Unfortunately, it was not

possible to examine them, and the presence or absence of rheumatism or recurrence of chorea are estimated from the subsequent histories obtained by a lady social worker. Where a history of subsequent ill-health was obtained this has been recorded as rheumatism.

In general, the subsequent histories show a gratifying absence of serious after-effects. For example, of the 10 boys, one is in the Royal Navy, one in the Royal Marines, one in the Merchant Navy and one was in the Royal Air Force. This last, however (Case 43), is the only one of the 34 who has died. He died early in 1945 of "heart trouble," after having served fifteen months in the Air Force. He had been passed fit on entry into the service. There was some doubt as to the condition of his heart at his last recorded examination at the hospital in the spring of 1937. The heart at that time was not appreciably enlarged, and no murmur was detected. But the pulse-rate was rather fast and there was a persistent reduplication of the second pulmonary sound. Two others have passed their medical examinations as fit for service with the Forces. The remaining 4 are not yet of military age. One works with a fish company, one is a ship's carpenter and the other two are still at school.

Of the 33 surviving patients of the follow-up group, only 3, all girls, now show evidence of ill-health and probably have residual heart lesions. Of these, 2 (8 and 23) are more or less chronic invalids and have had recurrences of chorea. The third is said to be "in fairly good health" but still nervous.

Of the remaining 21 girls, 2 are married and have babies and one is in the Women's Auxiliary Air Force. The others are either still at school or employed as maids, shop-assistants and the like.

Recurrences of chorea have been surprisingly few, only 3 of the 34 having had definite attacks of chorea since their discharge from hospital. Two of these are the invalid girls already referred to. The third (No. 15) is said to have had "several attacks" subsequent to her discharge, but none since she left school. Two others, one girl (No. 35) and one boy (No. 42) have residual fidgetiness when excited.

These results compare significantly with those of Sutton and Dodge (1938), who consider that "chorea should continue to be regarded not only as a manifestation, but as a major manifestation of rheumatic infection" and who treated it accordingly. They report that of 37 cases followed for from four to six years, "50 per cent." had recurrences. Wilson (1940), giving the findings in an aggregate series numbering 1138 cases in all, records that 47 per cent. were found to have undergone multiple attacks.

Gerstley (1935) reported that "since the organisation of the special clinic for chorea, we have had very few recurrent attacks from our patients who have attended . . . regularly. . . . The excellent results . . . indicate the importance of improved environment and mental hygiene in these patients." Markey (1936) expressed similar views, while Usher (1938) believes that "failure to direct our treatment along

these lines " (*i.e.* towards " the basic nervous constitution of the child ") " explains in great part the frequent recurrences which take place after discharge from hospital."

D. *History of Rheumatism in Siblings*.—Two of the 27 girls of the series had siblings who had suffered from rheumatism, one of whom had also had chorea. A sibling of one of the 15 boys had suffered from chorea.

(v) TOWN OR COUNTRY HOMES—URBAN OR RURAL.—Of the 42 children of the series, 34 were from homes in the city of Aberdeen and 8 from the surrounding country, that is from the counties of Aberdeen and Kincardine. Approximately 80 per cent., therefore, are children from city homes. It was felt that this figure might be weighted somewhat in favour of town cases by reason of the fact that the investigation involved one or more interviews with the parents at the hospital. However, on analysing the home addresses of the 131 children treated in the hospital for chorea from 1929 to 1942, it was found that 100 (77 per cent.) were from homes in the city of Aberdeen. It seems, therefore, that the special group is representative enough in this respect.

In the Report of the Committee on Scottish Health Services, 1936, the population of the city of Aberdeen is given as 167,000; that of the counties of Aberdeen and Kincardine combined as 180,000. While it is true that some country cases may be treated either at home or in Cottage Hospitals, it is unlikely that their number is high and there can be no doubt that the figures strongly support the accepted finding that chorea is chiefly an urban disease. If to the city children are added those who lived in street houses in country towns, the percentage rises to 87.

The total admissions to the hospital for the year 1945, exclusive of those admitted simply for tonsillectomy, was 2322, of whom 1191 (51 per cent.) were from the city of Aberdeen, 504 (22 per cent.) from country towns and 627 (27 per cent.) from the country.

#### 4. POPULATION DENSITY AND CHOREA

Bruce Perry (1937), in an extensive investigation of carditis in children in Bristol, found a significant correlation between the distribution of the cases and the density of the population in the different wards of that city. The above-mentioned 100 children from Aberdeen revealed a similar distribution. Fig. VI is a graph showing (a) the number of cases of chorea per 100,000 of the population, (b) the percentage of the population living more than two persons per room, and (c) the percentage living more than three per room, in the different wards of the city. Though the numbers are small, the graph shows a general correlation. Ward No. 11, with a low population density, shows a relatively high number of cases (6). Of the 6 cases from this ward, 5 came from one street which is situated in a slum clearance area and inhabited by people recently removed from the more crowded parts

of the city. Fig. VII shows a similar graph of the ten city wards left after omission of this exceptional ward and Ward No. 8 (a "west-end" one from which no cases were admitted), arranged in order of density of population. It will be seen that the case incidence from the five more crowded wards is more than twice that from the five less crowded. Hedley (1936) found the distribution of chorea roughly comparable to that of rheumatic fever, except that a more general distribution is indicated.

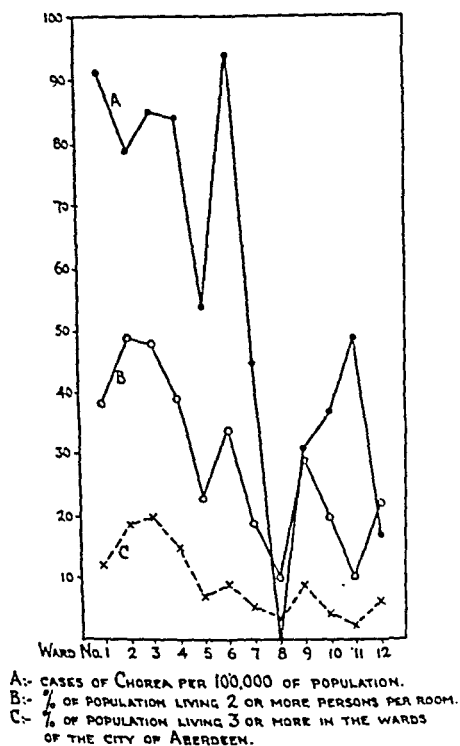


Fig. VI.

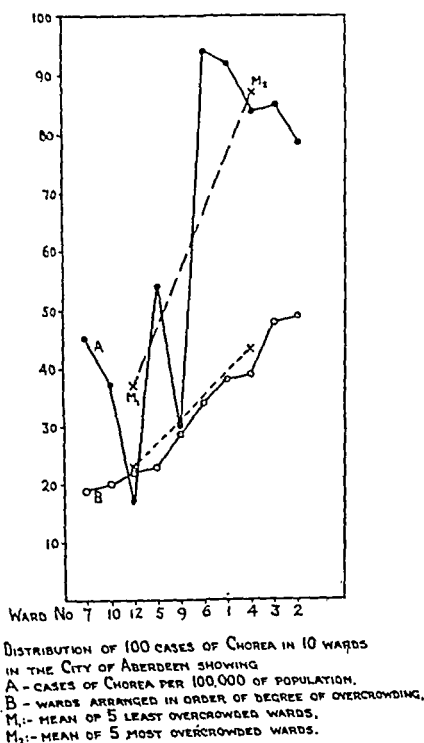


Fig. VII.

### 5. EFFECT OF THE WAR ON THE INCIDENCE OF CHOREA AND RHEUMATISM IN NORTH-EAST SCOTLAND

During the ten years 1930 to 1939 the annual average number of admissions for chorea to the Royal Aberdeen Hospital for Sick Children was 15.4. With the outbreak of war there was a spectacular drop in this figure, the annual average for the years 1940 to 1944 being 5. This last figure probably gives a slightly exaggerated picture of the fall in numbers, since a few mild cases were during the war period treated as out-patients who, under pre-war conditions, would probably have been admitted. A similar, though less pronounced drop occurred in the admissions for non-choreic rheumatism, the corresponding figures being 16.8 and 11.2 (Fig. VIII). During the 1930-1939 period the average annual number of medical in-patients



was 508; during the war period 1940 to 1944 it was 472. During the pre-war period the non-choreic rheumatic children represented 3.1 per cent. of the medical in-patients, and the choreic children 3.0 per cent. The corresponding figures for the war period are 2.4 per cent. and 1.0 per cent. (Fig. IX). Even allowing for the probable slight error attributable to the omission of mild cases treated as out-patients, these figures suggest that war conditions in the North-East of Scotland produced a situation in which children were less liable to develop chorea, whilst their susceptibility to non-choreic rheumatism

ADMISSIONS FOR CHOREA AND RHEUMATISM  
FROM 1930-1944 (INCL.) TO R.A.H.S.C.

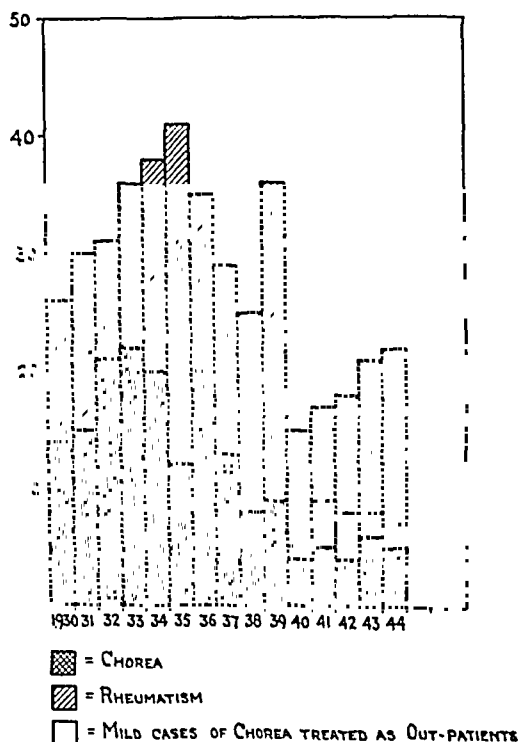


FIG. VIII.

PERCENTAGES OF CHOREA AND RHEUMATISM FROM 1930 TO 1944

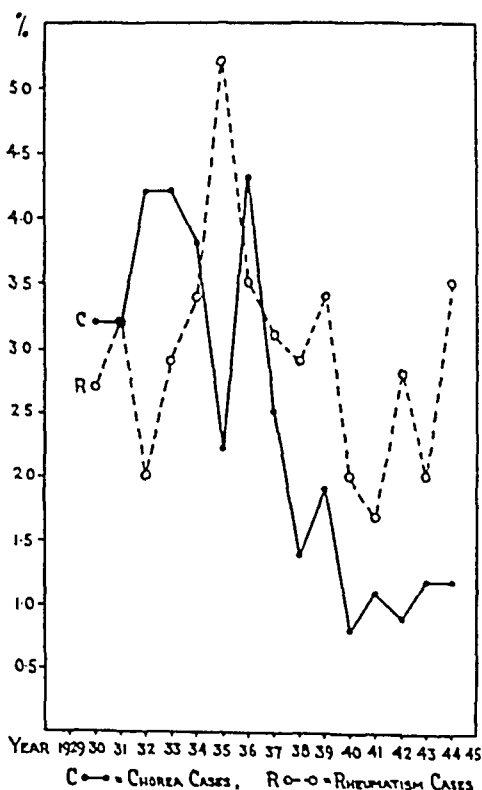


FIG. IX.

remained relatively uninfluenced. The percentage of non-choreic rheumatics among the in-patients in 1944 was actually above the pre-war average.

The absence of any marked effect of war conditions on the incidence of chorea was noted by Wall (1933) and others including F. J. Poynton, during the 1914-1918 War. It has commonly been held to support arguments against the psychogenic origin of chorea. In the light of information gathered in the present investigation this view would appear to derive from a misconception of the nature of the psychological hazards to which these children are subjected (Burlingham and Freud, 1942).

## 6. SPECIAL ANALYSIS OF THE SERIES

## A. NUMBER OF CHILDREN IN THE FAMILIES CONCERNED.—

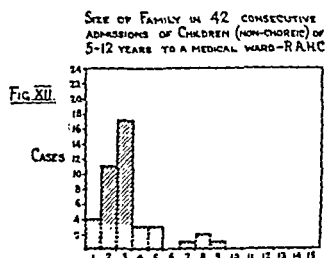
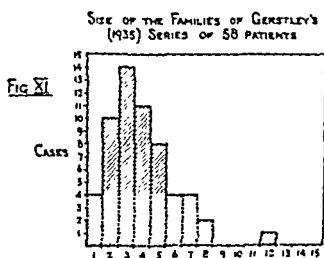
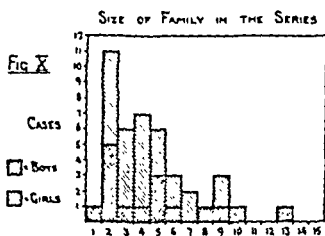
Fig. X shows the number of children in the families of the patients in the series. The fact that there was just one only child out of the 42 seemed rather unusual, though with this small number the finding may have no significance. A consecutive series of 42 children over the age of five admitted to a medical ward in 1945, showed four only children (see Fig. XII). Eleven of the choreic children were from families of two.

Gerstley (1935) records that in his series of 58 children there were 4 from one-child families. Fig. XI shows the distribution of his patients in relation to the size of the families from which they came. He does not give comparative figures of non-choreic children among the Chicago population from which his series was taken, but it will be observed that his figures, like those of the present series, show a high proportion of "large" families.

B. POSITION IN THE FAMILY.—A study of the position of the child in the family yielded some interesting and possibly significant information.

In 8 out of the 11 cases where there were only 2 children in the family, it was the elder child who was affected. On the other hand, among the 30 (affected) families with 3 or more children, only 4 eldest children were affected, all girls. In these 30 families there were, naturally, 30 eldest and 30 youngest children, and there were 86 surviving "middle" children. Eleven out of the 30 youngest children were affected, and 15 out of the 86 middle children. This apparent predilection for youngest children was found to be much more marked among the boys. In no case in the 9 families of 3 or more where the patient was a boy, was the eldest boy affected.

Investigating the position in the family of his 58 patients, Gerstley (1935) found that 20 of them were first-born, 15 youngest and 6 only children. This last figure does not tally with the number recorded in his "size of family" list. The discrepancy may possibly be explained by the inclusion in this list of non-surviving children. Forty-one out of the 58 "occupied positions in the family known to pædiatricians and students of behaviour as being hazardous."



C. MATERNAL FACTOR.—Normally no other single factor is so important in influencing the nature of a child as the quality of the maternal care. This factor was therefore particularly studied. It was not, of course, one which could be measured by any objective standard. The points postulated in the pro-forma were considered and a plus and minus method, based on the results, employed. Where the mother was judged to be of calm, stable temperament a minus was recorded. If she gave evidence of undue excitability, irritability, anxiety or other temperamental quality likely to engender in the child a feeling of apprehension or uncertainty, a plus was recorded, and when such quality was very marked, two pluses. In only 8 cases were minuses recorded, 4 each in the girls and the boys. In the remaining 34 there are pluses, and 9 of these are estimated at 2 plus. Of these 9, 5 were the mothers of boy patients.

In general, the impression gained was that the mothers tend to be anxious-minded women living under strain, usually over-conscientious and often with strong scholastic or social ambitions for their children. It is interesting in this connection that, referring to the difficulty of estimating and classifying maternal care the Medical Research Council Report (1927) says, "many careful, *anxious*, conscientious mothers, whose maternal care would be very good did their circumstances permit, must of necessity be undergraded owing to their being handicapped in this respect." It is debatable whether anxiety should be included among the desirable qualities in a mother. It seems possible that the prevalence of this quality may have a bearing on the common belief that the incidence of rheumatism and chorea is higher among the so-called artisan class than among the very poor.

D. PATERNAL FACTOR.—Although a number of the fathers actually attended at one or more interviews, in the majority of cases estimation of this factor had to depend on the mother's account. There seems little doubt that over the series the paternal influence played a less important role than the maternal. Eighteen, or nearly half of the fathers were almost certainly of even temperament and could not be considered responsible for anxiety or apprehension in their children. It was interesting that in a very large proportion of cases, enquiries on the subject of discipline elicited the information that this was left to the mother. Three of the fathers were marked 2 plus. Two of these were heavy drinkers and the third was a hectoring, bullying type of whom his children were definitely afraid. One was the father of a girl (Case No. 23), the others of boys (Cases Nos. 45 and 51).

E. FAMILY FACTOR.—In 30, or over two-thirds, of the cases there was a disturbing factor in the relationship of the child with one or more of the brothers and sisters. This was nearly always a matter of jealousy. It was probably always present in the two-family cases but has been marked minus in three of these, two of them boys with younger sisters (Cases Nos. 43 and 45); the third was Case No. 1 whose mother openly compared the child's scholastic achievements

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unfavourably with those of her sister. Although commonly occurring, this factor did not seem in any case to justify a 2-plus estimate. In no case did it seem to play more than a supplementary part.

F. ADVERSE HOME OR HOUSING FACTOR.—The main criterion in estimating this factor was overcrowding, though such points as distance from water supply and toilet, and attic or basement situation were also taken into account. No very high standard of house was required, but even so, 30 were assessed as plus and no less than 11 as 2 plus. In one case (No. 51) 4 children slept in one bed. In another (No. 41) 6 boys, the unemployed father and the mother lived in two rooms in an old slum house.

G. ECONOMIC FACTOR.—This factor, though naturally closely related to the last, did not necessarily accompany it, nor was it quite so frequently found, there being 25 pluses and only 4 double pluses. It might be absent in the presence of severe overcrowding, as in Case No. 6 where 7 children and their parents lived in a farm cottage but were relatively well-off in the essentials of life. In 2 cases (Nos. 36 and 39) it was present in the absence of marked overcrowding, in both cases the father being unemployed. In one case (No. 21) the weekly income for parents and 4 children at the time the child took ill was 27s. As might be expected, this too appears to be a supplementary factor aggravating others, notably the parental.

H. SCHOOL FACTOR.—This factor was found to be present much less frequently than was expected. This was interesting in view of the fact that it has been given considerable prominence in many investigations of chorea, Osler (1920) for example, speaking of the "so-called 'school-made' chorea." It is possible that this finding reflects the lessening severity of modern teaching methods, and this change of school atmosphere may have a bearing on the falling incidence of the disease.

Eighteen cases in all, 10 girls and 8 boys, were assessed with pluses. One girl (No. 15) and one boy (No. 46) have two pluses. In each of these, although there were also adverse home and economic factors, it was felt that the school factor—fear and dislike of the teacher in each case—was chiefly responsible for engendering a state of chronic anxiety and apprehension.

I. OTHER AND MISCELLANEOUS FACTORS.—In 9 cases, 7 girls and 2 boys, there were miscellaneous factors. These either concerned relations with neighbours or relatives outside the immediate family, or were connected with specific frights or chronic fear states. One girl (No. 31), for example, was terrified by a boy who chased her with a stick, and was afraid to go out and play whilst he was around. This child was aged five, the youngest of the girls in the series, and her illness began within a month of going to school where she was subjected to persecution by the same small boy and it is probable that this factor was an important one in her case. Usually this factor was associated with adverse home conditions.

## 7. SUMMARY OF THE SOCIAL AND PSYCHOLOGICAL FACTORS

Analysis of the environmental situation or life-background of these 42 children reveals that in no single case could it be said of the child that he or she was being brought up in a comfortable, decent home by stable parents unhampered by gross financial difficulties, and was leading a normal happy school life. The conditions to which these children were constantly subjected were such as might be expected to engender a state of chronic apprehension and anxiety. The child at this age has not the means of escaping from an intolerable situation that are available to the older child and to the adult.

## DISCUSSION

For over a century, ætiological thought on chorea has been dominated by the proven association of the condition with juvenile rheumatism. To certain minds, impatient of the requirements of strict logic, this seems to be sufficient proof of the causal relationship between them. Thus, in a well-known text-book, we read: "It is not now necessary to give the old statistics which proved twenty years ago that without rheumatic infection, there is no true chorea" (Wall, 1933). In another authoritative work it is written: "From all the available pathological evidence, chorea appears to be a meningo-encephalitis, a view which certainly fits in best with the clinical character of the disease and with its position as a rheumatic lesion" (Poynton and Schlesinger, 1931). In a third we find: "It is essentially a manifestation of rheumatic infection of the cerebral hemispheres" (Walshe, 1941). These quotations might fairly be taken to represent present-day teaching, at least in this country.

It is difficult to believe that dogmatic statements of this kind would have been made, had chorea continued to be studied, as it originally was, as a disease in itself, rather than as a form of rheumatism in childhood, or had not almost every study in recent decades started from the premise that along with carditis, arthritis, nodules, tonsillitis, and growing pains, chorea is one of the manifestations of rheumatism. Wall's pronouncement is simply question-begging; it is argument by definition. It would be quite possible to argue by this method that all pigs are white, by refusing to count as a pig any beast that was not white. The strength of this ætiological view is well illustrated in the first case in the present series. In the notes on the original examination, the physician in charge wrote: "Tongue movements, position of hands, *typically choreic*. Very fidgety with anxious strained look." Later, in a letter to the child's doctor, he wrote: "This is rather a doubtful diagnosis as there is a large psychic element in the case."

Recently a more judicial attitude has been taken. Thus, Wilson (1940) wrote; "For the better part of a century, since the original observations of Hughes and Sée, rheumatism has been recognised as

constituting a factor in the development of the disease, but the evidence, though abundant, needs sifting. Some assert an absolute causal relationship between the two, chorea being the symptom ; others accept their frequent coincidence with conceding a directly rheumatic origin for the nervous syndrome. Until the true nature of rheumatism itself is discovered, opinions on the interaction of the two will continue to vary." It is interesting to note that even in this cautious statement the last sentence almost implies an acceptance of the causal relationship. McNee (1940), in a critical survey, says : " There is still . . . a want of positive knowledge of the commonest cause of cardiac disease in youth, for the ætiology of rheumatic fever and chorea escapes us."

Bruce Perry (1937) writing in another, though related connection, points out that " it is impossible to argue from observed association to actual causation . . . observed association is the starting-point and not the end of research."

There are formidable arguments against accepting the causal relationship of the two conditions, and its more thoughtful proponents have recognised this, and are not dogmatic. Thus, Cheadle (1897) considered that " the presumption is strongly in favour of the view that, in the great majority of cases, at all events, chorea is of rheumatic origin." Purves Stewart, writing in 1906, pointed out that " The results of (post-mortem) examination may be negative, the brain, spinal cord, and peripheral nerves appearing absolutely normal—so far, at least, as the present methods of neuro-pathological research enable us to judge," and concluded, " It is not at all improbable that chorea in many cases may be due to a toxin, probably closely associated with the rheumatic toxin, if not identical with it."

Osler (1920), after listing seven points which *suggest* but do not prove an infective origin, concludes in a similarly guarded phrase, " It seems not improbable that it is a form of infective encephalitis with a special localisation."

Risien Russell (1899) is even more cautious. In discussing the pathology, he writes : " Fascinating as is the hypothesis of the infective origin both of acute rheumatism and chorea, it is far from proved ; and the same may be said of our knowledge of the affinities of the two diseases. There are many facts in the causation of chorea which demand careful consideration before we hastily accept any such generalisation."

Nervous instability is noted by all students of the disease, but its ætiological significance has been interpreted in widely different ways. The difficulty which confronts those who accept the toxic-infective theory of the pathogenesis is to determine whether this nervousness is the cart or the horse. "Chorea," says Wall (1933), "is essentially the manifestation of rheumatism in the neurotic subject. The instability of the nervous system may be inherited, or may be acquired through illness, fatigue, excitement, and so on. Rheumatism invariably has



some effect on the nervous system of a child, rendering it unstable, excitable, and emotional, and, therefore, it is difficult to determine how far the so-called predisposing causes are truly causative. Undoubtedly for the most part they are not active in originating the chorea but merely unmask or exaggerate a chorea already present in an incipient stage. Fright, for instance, is often given as a cause of an attack of chorea; but in most instances the child does not develop chorea because it has been frightened, it is frightened because it is already in an emotional state of early chorea, and the disorder is thereby unmasked." Similar, though usually less emphatic views, have been expressed by nearly all writers in text-books and monographs until quite recently, amongst others by Hempelmann (1925), Poynton and Schlesinger (1931), Holt and Howland (1931), Lapage (1933), Pearson (1939). Poynton and Schlesinger draw attention to one well-authenticated fact which is hard to explain by this hypothesis. "Why a child with an unstable nervous system should be liable to rheumatic infection, and if so, why it is not more frequent among the well-to-do, are questions not easily answered."

The conclusions of Neustatter (1937) are significant in this connection. They include the following:—

- " 1. Nervousness is not greater in joint rheumatism than in other illness or in general debility, but is significantly greater than in normal children.
- " 2. The high total of nervous features observed in rheumatism is due to the very high incidence of such features in chorea, and in children who come under observation only from 'pains.'
- " 3. As nervousness is present in a significantly greater proportion of children before the age of two, who are later nervous, the nervousness is not a rheumatic manifestation. The rheumatism may aggravate the nervousness, but does not cause it. There is probably a common diathesis for nervousness and rheumatism."

Neustatter also considers that "there is suggestive evidence that bad home conditions may play a part in producing nervousness."

The general impression left by a study of the literature on this subject is one of inconclusiveness and uncertainty. The arguments of those who definitely accept and proclaim the toxic-infective hypothesis smack of special pleading; they could not be described as scientific deductive reasoning from proved data. In any case, as Hubble (1943) says, "the facts concerning chorea do not support any theory that chorea is directly due to the rheumatic 'invader' or to 'rheumatic toxæmia.' " It is clear that in its straightforward form of postulating a specific rheumatic bacterial toxic agent operating in the child's blood or tissues to produce acute rheumatism or chorea or both, the hypothesis

must be rejected. All the known signs of toxæmia may be absent in chorea. To explain this it is sometimes suggested that chorea in itself is indicative of a mild infection (Duckett Jones (1935), Ashe (1936)). If this be accepted, however, it becomes difficult to explain why, since the greater includes the less, every child with rheumatic fever does not at the same time have chorea. To get over this difficulty it is necessary to postulate that this comparatively light infection is working under the special conditions of a child with a peculiarly sensitive nervous system. We are thus thrown back once more on the necessity to explain this unusual nervousness.

Two recent trends in medical thought have operated during the past ten or twelve years to loosen the hold of this traditional attitude to the problem of the ætiology of Sydenham's chorea. These are first, the growing appreciation and understanding of the part played by psychosomatic disturbance in the production of physical symptoms and functional disorder and, more recently still, the biological emphasis in the ætiological concepts of what has come to be known as social medicine. Both of these approaches to the problems of ætiology are broader and cast wider than the older systems which attempted always to narrow down the search in the hope of being able eventually to point the accusing finger triumphantly to the incriminated agent. They are the outcome of the growing acceptance of the view that health and disease, though they may be regarded conceptually as opposites and antithetic, are in reality but opposite ends of an infinitely graded scale; that the state of health of an individual at any time is, as it were, the measure of his success in reacting to his total environment. A system of ætiological study based on such a concept demands the widest possible investigation of the total environment, both internal and external, past and present.

Reports of investigations of this type in relation to the problems of chorea began to appear about a dozen years ago. Walker (1935) enquiring into the social environment of 188 cases found 65 to come from families living seriously below proper subsistence level, and noted that there appeared to be "a definite relationship between population-density and chorea." Some years earlier the Medical Research Council (1927) had published its Special Report of a large-scale investigation of "Social Conditions and Acute Rheumatism," in which "Rheumatism" was taken to be "Acute Rheumatism with its recognised manifestations, chorea, organic heart affection and nodules." This investigation supported the frequently expressed view that highest incidence is found not among the lowest income group but in those slightly above this level. (The distribution of the Aberdeen cases is in line with this view so far as chorea is concerned, see Fig. VII.) On the other hand, during a discussion on "the ætiology of acute rheumatism and chorea in relation to social and environmental factors" in 1934, J. A. Glover expressed the belief that the true incidence of acute rheumatism is directly proportional to the degree of

poverty and suggested that a larger proportion of the least resistant among the very poor fail to survive to the rheumatic age. Coburn and Moore (1937), analysing a series of 114 cases of chorea, followed monthly for from two to ten years, and a consecutive series of 137 cases admitted to hospital, found that in one-half of these cases the "attacks were not preceded by respiratory infections, but seemed to be associated with psychic trauma." Hubble (1943) brings under review these various findings and observations on social status in relation to rheumatism and chorea. After referring to the Medical Research Council's classification of the families in its investigation (1927) into three economic groups, in inverse order of poverty, as Groups A, B, and C, he writes: "No observer has suggested that the mental and nervous stresses of poverty on children may be as important as the physical. It needs little imagination to see that the nervous stresses of poverty will be greater in Group B than in Group A or C, greater than in the less poor and in the more poor—that is, in the family which has known failure and is pre-occupied with the fear of failing again, with its struggle to keep up appearances, with its avoidance of social life, with its emphasis on hard work as a prelude to success, and with the distortion of its emotional life by fear and insecurity; this is the domestic background to Group B families. Is it fantastic to see in this environment one of the breeding-grounds of child rheumatism? In which class should we expect to find that education imposes a greater nervous strain? Although this factor of nervous instability may explain the higher incidence of rheumatism at this particular economic level of poverty, the general association of rheumatism with poverty at all levels probably depends, as a host of observers have assumed, on the physical accompaniments of poverty, poor clothing, bad and damp housing, malnutrition, and overcrowding. While most of these factors operate by reducing the resistance to infection, others such as overcrowding presumably act by increasing the number and virulence of nasopharyngeal infections."

A general conclusion which it would seem justifiable to draw from such findings and observations is that certain factors commonly but not necessarily associated with poverty play an important part in the genesis of chorea (and juvenile rheumatism).

The present investigation strongly supports such a conclusion and suggests that so far as chorea is concerned, these factors are of a psychological rather than a physical nature. It is difficult to explain otherwise the finding in every one of 42 cases of life situations calculated to induce in the child a state of long-continued nervous strain and apprehension, and that management based on the appreciation and amelioration of this situation was followed by a recurrence rate markedly below that usually experienced.

Our modern realisation that physical changes are frequently induced by purely psychological disturbances makes it less difficult than it was thirty or even twenty years ago to accept a psychogenic origin

for the physical concomitants of chorea, both the hyperkinesis and the muscular hypotonia. Electro-encephalographic investigation has not demonstrated any very constant finding in cases of chorea, but has frequently shown irregular areas of cortical hyperexcitability, commonly localised in the central region contra-lateral to the maximum motor disturbances (Buchanan *et al.*, 1942). Modern neuro-anatomical studies have demonstrated the very close integration of the so-called pyramidal and extra-pyramidal systems and the existence of intricate circuits passing from the cortex to the basal ganglia and back again (Mettler, 1942). Wilson (1928) many years ago postulated that chorea must be attributed to the disorder of a system and commended Hughlings Jackson's concept of "physiology in difficulties." That a destructive lesion of a part or parts of these systems can produce the movements of chorea has been proved beyond doubt in the case of Huntington's chorea and of many examples of senile or arterio-sclerotic chorea, but that such a lesion is necessary to their production is very simply disproved by the fact that they can be produced voluntarily without any difficulty by any healthy person. That functional disorder should result from prolonged affective disturbance is not only possible but even probable. Exhaustion of the striatum or globus pallidus are likely to produce results similar to if not as profound as destruction of them. It might in fact be expected that they would produce the release phenomena of striatal elimination and loss of large-muscle tone of pallidal origin in just the degree to which we find them in children with chorea. The gradual passing of these features which marks recovery from the illness would naturally follow recovery from the exhaustion.

From all these considerations it seems possible to adduce a valuable clue as to the nature of the "humour" which Sydenham postulated, whence it is derived and how it acts. It can be regarded as an affective disturbance induced by subjection to psychological stresses from which the child can find no satisfactory escape. If this disturbance is sufficiently severe or long-continued it produces the hyperkinesis and hypotonia which are characteristic of the established disease, very probably through cortico-thalamic exhaustion.

This hypothesis is consistent with the age, sex and social incidence of the disease. Its validity is supported by the success of treatment based upon it, and by the quite common absence of any of the known signs of infection in undoubted cases. It provides a very probable explanation of the falling incidence of chorea and of the relatively much greater fall as compared with that of juvenile rheumatism, for, while the physical lot of the "rheumatic" classes—apart perhaps from improved diet—has not undergone any marked amelioration, there has in recent years been a very real advance in the understanding and management of children, both at school and at home. It is uncertain whether this fall was influenced by war conditions since it had already begun two or three years before the outbreak of war,

but we should expect the lessening of neurotic illness which accompanies the external pre-occupations of the state of war to have some such effect (Burlingham and Freud, 1942).

Most important of all the hypothesis sheds light on the central problem—the nature of the association between chorea and juvenile rheumatism. The link between them in all probability is that their causes commonly but not necessarily occur in conjunction as concomitants of poverty and overcrowding. Exposure in varying degrees and at varying times to these two sets of causal factors, the one physical and the other psychological, we should expect to give rise to an incidence of the two conditions, such as has been revealed by many and careful observations, so that some children so exposed will develop chorea, others rheumatism and others again both, either concurrently or at intervals of time. We should expect, as we find, that the child debilitated by latent or overt chorea will be more likely than his tougher brother or sister to succumb to the factors which give rise to rheumatism. That chorea causes rheumatism is probably nearer the truth than that rheumatism causes chorea.

#### SUMMARY AND CONCLUSIONS

1. The history of medical opinion on the ætiology of Sydenham's chorea over the two-and-a-half centuries since he described it has been briefly reviewed.

2. It is pointed out that, although much has been learnt of the condition, no generally acceptable theory of the nature of the "humour," to which Sydenham conjecturally ascribed it has as yet been forthcoming.

3. The hardening of opinion in favour of a toxic-infective theory, which followed on the development of bacteriology, is shown to be unjustified.

4. Certain sociological factors in relation to 131 children treated for chorea in the Royal Aberdeen Hospital for Sick Children between 1930 and 1942 have been considered, and the influence of war conditions on the incidence of the disease in the North-East of Scotland.

5. A more thorough and detailed investigation into the life circumstances of 42 of these children is recorded, which revealed that in every case the child was subjected over a considerable period of time to conditions calculated to induce functional nervous disturbance.

6. The results of these investigations are shown to be similar to those of recent investigations of the same kind by pædiatricians both in this country and in North America, and to support the conclusion reached by many of these investigators that chorea is probably a psychologically determined disease.

7. It is suggested that we now have the clue to the nature of Sydenham's "humour." It can be regarded as an affective disturbance induced by subjection to psychological stresses from which the child can find no satisfactory escape. If this disturbance is sufficiently severe

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<sup>1</sup> Vilter, W. et al. (1946) J. Lab. Clin. Med. 31, 609.

<sup>2</sup> Zuelzer, W.W. and Ogden, F.N. (1946) Amer. J. Dis. Child, 71, 211.

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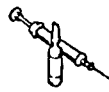
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or long-continued it produces the hyperkinesis and hypotonia which are characteristic of the established disease, very probably through cortico-thalamic exhaustion.

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# ELECTRO-SHOCK AND ELECTRONARCOSIS IN THE TREATMENT OF MENTAL DISORDERS \*

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THE subject of this lecture is to discuss recent developments of certain new methods of treating mental disorder. It was said by an American commentator last year (Bennet, 1946): "Never before in psychiatric history has an innovation stimulated such wide research in the therapeutics of mental illness as have the modern physiological methods of Sakel and Meduna (insulin coma and electro-shock). . . . The success of improved treatment has aroused new interest in psychiatry as a field of medicine."

Before the advent of these therapies, when one had observed the psychotic patient over a period of time and found that he was failing to progress, or even continuing to deteriorate, there was nothing much more that the medical officer could do. He could only employ conservative methods of treatment hoping that a spontaneous remission would set in. So much was this so that nothing was more welcome to the psychiatrist of fifteen years ago than to find that a case which had seemed at first to be a functional psychosis, was in fact a case of organic disease of the nervous system for which an effective remedy had already been discovered. I well remember when at the Royal Glasgow Mental Hospital, under Sir David Henderson, I examined a stuporose woman who showed no clear neurological signs of disease. Her sole occupation was pulling out her own hair. When it was found, however, that her C.S.F. showed the typical signs of general paralysis, she was infected with tertian malaria and later given tryparsamide. She made a permanent recovery within a matter of weeks.

Treatment of the functional psychoses, however, (schizophrenia and the manic depressive psychosis), had been improved only in the later stages of these disorders, if a spontaneous remission had set in. One then tried to rehabilitate the patient to the outer world by means of occupational therapy, communal recreation, and psychotherapy; and also by the employment of social workers who could investigate home conditions.

Nevertheless I remember in 1930 two events which seemed to indicate that one might in time produce results in the case of the functional psychoses which would be just as dramatic as in the case

\* A Honyman Gillespie Lecture given in the Royal Infirmary, 16th October 1947, illustrated by a cinematograph film.

of general paralysis. On one occasion I was fortunate enough to witness what Adolf Meyer would call an experiment of Nature. A schizophrenic woman developed erysipelas from which she very nearly died, and when she recovered from her erysipelas, it was found that she had also recovered from her schizophrenia.

This seemed to indicate that a physiological condition like fever and confusion could alter the course of a psychosis. I remember thereafter giving injections of sterile sulphur to produce fever in a rapidly dementing girl in the hope that a similar remission would occur. She did in fact become perfectly sane and rational as long as her temperature was high; but the effect unfortunately was only temporary. French psychiatrists, however, still use artificial pyrexia at the present time as an adjunct to electro-shock (Delay, 1946).

Another striking event in 1931 was at the Phipps Clinic, Baltimore, when we gave 15 per cent. carbon dioxide in oxygen to a schizophrenic who had been mute and stuporose for eighteen months. Yet for twenty minutes after inhalation of the gas he became perfectly rational and talkative, before once more relapsing into a stupor deeper than before. Here again an alteration of the physiological state had interrupted the psychosis. Incidentally, this gave rise to further research into respiration in mental disorders (Paterson, 1934, 1935).

It was only at a later date that certain lines of investigation gave grounds for hope that early treatment of the psychoses by certain physical means would produce a remission earlier than would otherwise have occurred.

### THE ADVENT OF "SHOCK THERAPY"

The scientific enquirer may take as his motto "Seek and ye shall find," but the curious thing is that he often finds something quite different from that for which he was originally seeking. Christopher Columbus looked for India but discovered America. Thus Meduna (1939), in the belief that the schizophrenic and epileptic reactions of the organism might be mutually exclusive, initiated the treatment of schizophrenia by convulsant drugs. While the effect on schizophrenia, however, was limited, the treatment was found to be particularly successful in melancholia.

Again, Sakel in Vienna in 1927 conceived the idea of treating those addicted to morphine and other drugs by administering large doses of insulin. The method, however, appeared to produce more striking results in schizophrenia than in addiction.

In 1939 Professor Ugo Cerletti, working with Bini, showed that it was feasible to cause a convulsion by means of electricity. This method had several advantages over that of Meduna. It was easier to give; the patient instead of having the distressing experience of going off into a fit while still conscious, as with cardiazol, could now feel nothing at all. Further, the pull of the muscles was less powerful so that there was less chance of a bone being fractured. It was also more

convenient and quicker to administer. With cardiazol it had sometimes been impossible to complete the treatment because an obese patient with small veins could not be given any more injections. In every way electro-shock proved a less crude mode of treatment than the administration of cardiazol.

The following case history will illustrate the dramatic recovery of a patient who would undoubtedly have continued to deteriorate if she had not had this type of treatment. The benefit which she received is all the more striking when we consider the degree of the patient's distress. As one such patient said, "Last night I was wrestling with all the devils in hell, but to-day I am at peace."

Mrs A. aged 61, was the wife of a druggist and was first seen in 1945. She worked in the shop and kept the accounts. Three years previously she had begun to suffer from obsessional thoughts of a distressing kind. Obscene words kept coming into her mind and this worried her. She felt that she must be very wicked and that God was angry with her. She slept very little, ate little and had lost 11 lbs. in weight. She had a chronic bad taste in her mouth. She became obsessed with the idea of the poison cupboard in her shop and was afraid that she would take her own life. Describing her illness, she said, "I am terribly depressed. I have no pleasure or interest in my work. Some sinister influences are at work and are affecting my mind. I have tried Christian Science but that has not helped me. They only told me that I must not go to a doctor!" She used strange expressions and said that she was "up against a malpractice that was going on."

She was given six electric convulsions, and her depression and feelings of influence and obsessions completely disappeared. She ate and slept well and put on weight. Whereas before she had been unable to add up and do her accounts, she now found this perfectly easy. In answer to enquiries two years later, she said that her recovery had been maintained in every respect.

The following case shows that a completely different reaction pattern of the nervous system can be dispersed by this same treatment:—

Mrs B., a professional violinist, and a widow, aged 58, visited me on 31st May 1946 suffering from mania so that she could no longer remain at home. She was restless and got up at night, walking about the streets at all hours, laughing in an uncontrolled manner and unable to stop talking. She became enamoured of a plumber who came to do a job in her house and she gave away a large sum of money to a soldier. She was determined to publish a song written by her father and broadcast it, and would talk of little else.

A year previously she had been in a mental hospital for nine months without having special treatment. On the present occasion, however, she became completely well in a few weeks after having 12 treatments with electro-shock.

The following is a case of refusal of food accompanied by delusions that her food was not passing properly through her body. This patient had failed to benefit from the usual medical treatment in hospital.

In the past three years Miss C., aged 24, had lost nearly two stones in weight, and amenorrhoea had been present for two years. Her symptoms had started

when she had been jilted by a soldier while in the A.T.S. She developed an obsession about mucus in her nose, and read in a book that a starvation diet with less carbohydrates would cure it. She gradually came to eat less. She welcomed her loss of weight because she wanted to reject the signs of womanhood, and for two years she had not menstruated and the prominence of her breasts ultimately disappeared. She developed an idea that food would not pass through her. Being a tall girl, she felt conspicuous and thought that people were looking at her and laughing at her.

A thorough examination, including an X-ray of the stomach and lung fields and fasting blood sugar, showed nothing physically abnormal.

*Treatment.*—After she had told the story of her disappointment at being deserted by her lover, and an attempt had been made to make her change her outlook, no alteration in her condition occurred. Neither insulin before meals, nor endocrine therapy affected her. However, after 8 treatments with electro-shock in fourteen days, her whole outlook changed. She began to eat well.

During her convalescence she was given 100,000 units of oestroform once a week for two weeks, followed by ethesterone 5 mgs. for eight days. She was also given a protein preparation called casydrol and half a grain of thyroid a day. She gained two stones in weight. Her menstruation returned and when last seen, she was the picture of health and working well.

That even cases of paranoia can completely recover with electro-shock is shown by the following case.

Miss D., aged 43, was first seen on 13th March 1946. For seven years she had had a love-affair with a man of 60 years of age. He would have married her, but his wife, who was 80 years of age, was in a mental hospital with alcoholic dementia. For three years the patient had believed that people were accusing her of being a prostitute and she sometimes thought she heard people saying this. Wherever she went she felt that persons in the street were talking about her. She developed terrifying delusions that she was going to be dragged away, tortured and killed. She believed that she was contaminating people and spreading disease. There was, she thought, a recording apparatus in the next room which was taking down everything she said.

The patient was given 10 treatments with electro-shock, after which her delusions and depression completely disappeared. She was also given advice about changing her mode of life so that the conflict which had apparently given rise to her illness, was resolved.

Eighteen months later she and her relatives reported she was still well and at work and symptom-free.

### CRITICISMS OF ELECTRO-SHOCK

Despite the dramatic recoveries which have been obtained by electro-shock, criticisms have not been wanting. The secretary of the Electro-Shock Research Association of America, in reviewing the present position this year, writes as follows: "Shock therapies are now being evaluated and revised in the light of several years' experience. The complications, relapses and failures have tempered the early enthusiasm."

One authority (Salzman 1947) has stressed the fact that in patients who have relapsed after shock treatment there have been occasionally some slight signs of mental deterioration, such as emotional flattening and apathy, memory defect, and even lack of attention to personal habits.

The reason for this is no doubt that in America many patients with schizophrenia, or even melancholia, have been treated with as many as twenty or even forty convulsions. It is also true that some of the instruments used allow a much higher current to pass through the brain than those used by some of us in this country. The instrument used by us does not allow of a current of over 250 m/A (Paterson, 1945, 1946).

A questionnaire which we recently sent out to the first 80 patients treated at the West London Hospital, satisfied us that this therapy was justifiable in selected cases, which would not clear up with conservative treatment. Many of these we would ordinarily have sent on to local mental hospitals, but these have been overcrowded and unable to admit voluntary patients.

From the answers to the questionnaire it appeared that 75 per cent. were able to return to work after the treatment, and in 80 per cent. of cases the patients' families stated that they had improved. These figures, however, scarcely do justice to the success of the treatment. The answers in many cases expressed the greatest gratitude for relief from an intolerable and long-standing illness. Seventy-seven per cent. said that they slept better and were not so tense. Seventy-three per cent. said they would advise others with similar symptoms to have the treatment.

In reply to a request for criticism of the treatment, 15 per cent. suggested that it would be kinder to give an anæsthetic before the treatment. Twenty-three per cent. complained of temporary memory defects, but in no case was this permanent. Five per cent. complained of back-ache. One of these had concealed the fact that he had previously injured his back through attempting suicide by throwing himself from a two-storey window.

In eight years' experience I have not had any death from the treatment. The chief hazards have been compression and fractures of a spinal vertebra, which, however, generally cease to give trouble after a few weeks without any specialised treatment being given. In no case was there permanent disability.

These figures quoted show that electro-cerebral therapy has been an important addition to the methods used in the psychopathic unit of a general hospital.

#### RECENT IMPROVEMENTS

The problem before us has been to find a form of treatment which would be as effective as possible but which would provide the minimum of discomfort and the minimum of subsequent risk for the patient.

We have found that the administration of pentothal before treatment removes the patient's apprehension. It also prevents restlessness when he subsequently wakes up, and in cases where curare is given, pentothal prevents the uncomfortable feeling of paralysis which is present. The administration of curare has enabled us to treat patients who have, for instance, a damaged heart or a back injury, or who are elderly and obese.

Another important line of research has been directed towards providing an electric current which would produce a maximum therapeutic effect while being well below the threshold at which damage would be caused to the patient's brain.

### THE HISTORY OF ELECTRONARCOSIS

The first investigator to use electronarcosis was Stéphane Leduc of Nantes, who, at the beginning of the century, employed a uni-directional pulse current with a square-shaped wave which had a frequency of 100 per second, the relationship of the wave to the interval being 1-9. A current of only 1-8 m/A was employed. Leduc placed the anode on the sacrum and the cathode on the vertex of the skull. He could in fact use only a small current because the heart muscle was included in the circuit.

He allowed the current to be applied to himself, and although he did not become unconscious, he was unable to move or speak, and later described himself as having been in a dream-like state.

In 1910 Leclerc described two operations, one lasting ten minutes and the other fifty minutes, in which the patients were anæsthetised by this means. He mentions that Tuffier had also used this procedure as an anæsthetic.

Van Harreveld, working first in Holland and later in California, has shown that if the electrodes are placed on each temple, electro-narcosis can be produced by means of an alternating sinusoidal current such as can be got from the mains. The margin of safety is greater because the heart is not included in the circuit.

In 1946, having read of van Harreveld's researches (van Harreveld and Kok, 1934; van Harreveld *et al.*, 1943) and also of his psychiatric collaborator, Dr E. B. Tietz, we availed ourselves of the help of Messrs Shotter and Rich, who constructed a serviceable machine for clinical use.\*

### COMPARISON OF ELECTRO-SHOCK, ELECTRONARCOSIS AND CONTROLLED ELECTRO-SHOCK

The accompanying diagrams illustrate the differences between electro-shock, electronarcosis and controlled electro-shock. The last-named is carried out by means of an electronarcosis machine. In Fig. 1 the shaded panel represents the current passing through the patient's

\* This is obtainable from Messrs Rich and Bundy, Ltd., 18 New Road, Ponders End, Middlesex.

# Comparison of Electro-shock,Electronarcosis and Controlled Electro-Shock.

Chart showing muscular reaction to current variations in relation to time  
(after Tietz, Olson & Rosengoff.)

## ELECTRO-SHOCK Less than one second.

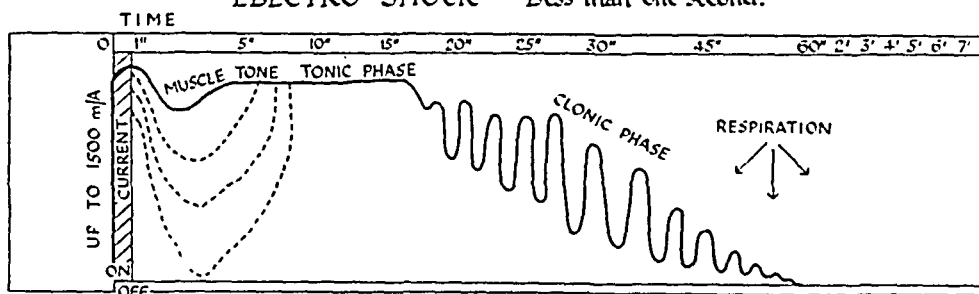


FIG. 1

## ELECTRONARCOSIS

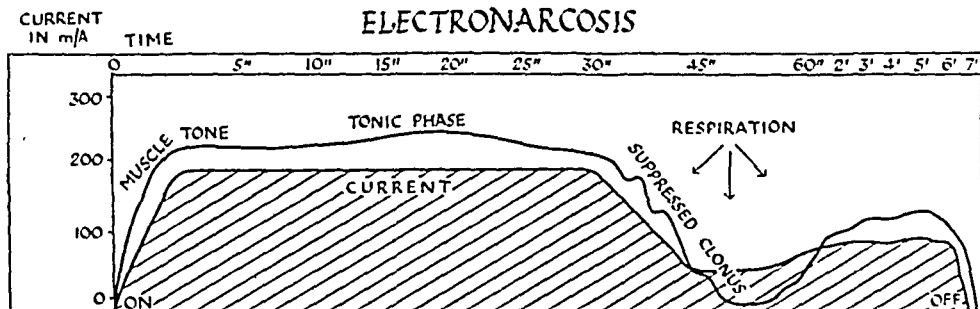


FIG. 2

## CONTROLLED ELECTRO-SHOCK.

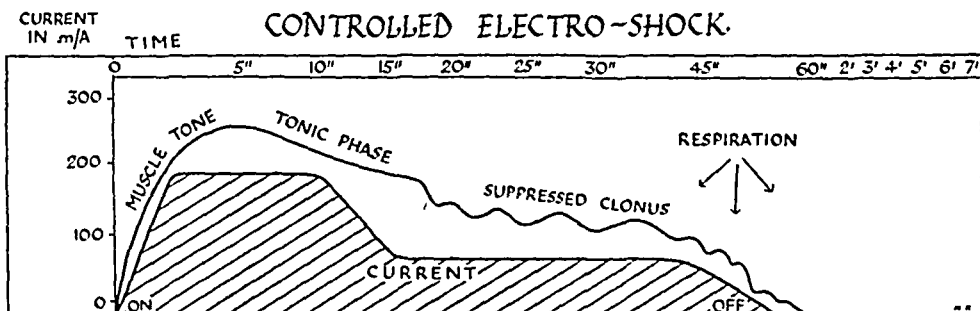


FIG. 3

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brain. This varies according to the type of machine. In the condenser type, a current of some 1200 to 1500 m/A passes for a small fraction of a second. In some machines it is stated that "it is impossible for a current of more than 2000 m/A to pass through the patient's brain." In our electro-shock machine (Paterson, 1944), however, a current of under 250 m/A is passed generally for about half-a-second.

The continuous line shows diagrammatically the degree of muscle tone. This fluctuates during the experiment, being maximal at the beginning, and decreasing to a varying degree (dotted lines) for the first seven seconds, but never quite attaining its former height. After fifteen seconds, clonic movements commence and the tone decreases until forty-five seconds from the start, after which respiration becomes fully established.

In Fig. 2 (electronarcosis) the current starts at zero and in the course of three seconds rises to about 200 or more m/A. The fact that we start at zero and take three seconds to reach the maximal current, prevents that sudden pull of the prevertebral muscles, which in electro-shock may cause compression of a vertebra. The current is then kept in the neighbourhood of 200 m/A for half-a-minute. At the end of that time the current is slowly allowed to fall to 90 m/A. This slow reduction in current prevents violent clonic movements, which in the past have occasionally caused a fracture of bone or dislocation.

Respiration then occurs at the same point of time (about forty-five seconds) after the commencement of treatment as in the case of electro-shock. Thereafter the current is slowly raised to about 110 to 140 m/A according to the physiological signs. These should consist of a moderate degree of flexion at the elbows and a slight respiratory stridor.

The current is brought down to zero, again in three seconds, at the end of seven minutes.

The treatment is given three times a week with a minimum of eight treatments, but as many as sixteen treatments may be given. (For a fuller description of the technique, see Paterson and Milligan, 1947.)

Fig. 3 shows the treatment known as controlled electro-shock. It will be seen that here again the current is passed through the brain in a gentler manner, taking three seconds to attain its maximum. The relatively small current is passed for about seven seconds and again gradually reduced to 90 m/A and kept there till forty-five seconds. The muscular tonus again suppresses violent clonic movements and respiration recommenced at the same point of time as after ordinary electro-shock.

In our experience, side effects such as loss of memory for recent events and headache are less frequent and where they occur, much less severe in electronarcosis and controlled electro-shock than where the old technique is used. Many patients state that they have experienced no discomfort whatever from these forms of treatment.

## CLINICAL EXPERIENCES WITH ELECTRONARCOSIS

Several cases have cleared up with this treatment after electro-shock had failed. This is important because in such cases the next step hitherto has been for the psychiatrist to consider the operation of leucotomy. The two following cases are examples :—

Mrs E., aged 47, was first seen on 31st July 1947 complaining of depression for eighteen months. She was at the menopause. Her periods had been irregular and she was suffering from hot flushes. She had had a number of worries. Her father had died, her mother had become mentally ill and she had had a love-affair during the war with a man other than her husband.

She said that people were talking about her and saying that she was immodest. At times she had attacks of panic when she could not bear to have a knife near her in case she should injure her husband, her daughter or herself. She was also afraid to go near a window in case she should jump out. She was not sleeping or eating well and she was afraid that she would take her own life. Further obsessional thoughts came into her mind that she might poison her husband without meaning to do so.

*Previous History.*—She had always been a very energetic woman and fond of social life. Her husband was ten years older and was quiet and under-sexed, a fact that had caused some difficulty in adjustment.

*Family History.*—Her mother had twice had attacks of depression lasting six months.

The patient was given 9 treatments with electro-shock. She was a little less depressed but her obsessional thoughts of knives and poisoning remained. When examined, she was still in a state of the greatest agitation and wild-eyed panic. She was given electronarcosis with dramatic results. She said, "This is something quite different. The effect of removing the unbearable tension is so complete." After 6 treatments, she became quite calm. She said that the nightmare had passed; she had no more obsessions or panics and she appeared happy and contented.

Another case which has cleared up with electronarcosis after electro-shock had failed, is the following :—

Mrs F., aged 41, was first seen on 14th May 1947. She was confused and had delusions that her food was being poisoned. She had been very depressed for a year.

*History.*—Thirteen years previously she had married a man twenty-three years older than herself because she was very fond of the man's child. The marriage was never satisfactory from the physical standpoint, and the patient threw herself into business activities. She built up a business as a middle-man in the hardware trade. She had a happy relationship with her senior partner and business prospered. During the past year, however, difficulties had arisen between herself and her partner and it became obvious that he wanted to part company. From being over-active and energetic, she became moody and depressed and finally after refusing food, she became paranoid and confused. She was actively suicidal and had made two attempts before she was first seen.

After having been given sedatives and good food, her confusion had nearly disappeared and she was given 8 treatments with electro-shock. She

appeared to be somewhat calmer but when her general situation was discussed, she said that her marriage was a failure and her business ventures had come to nothing and that she was resolutely determined to end her life as soon as she left hospital.

She was given 4 treatments with electronarcosis and she said that she now felt greatly relieved and quite calm. She had lost her suicidal urge and she had confidence that she would be able to return to work as plans had already been maturing in her mind. She attributed her recovery entirely to the second type of treatment (electronarcosis).

After a period of convalescence and rehabilitation, she appeared to be restored to her previous state of health.

We have had some success in treating schizophrenia.

For instance, Miss G., aged 25, was first seen on 6th December 1946. She was a hospital nurse who had previously won medals for swimming and running. She had been ill for five weeks. When examined, she had curious mannerisms. She walked with a dipping gait as if she were curtsying. She looked pale and thin and was completely self-absorbed. She kept moving her denture up and down in her mouth and moved her knees in and out in a rhythmical manner. Her mother said that she kept talking aloud and the patient complained that everything seemed different. She would lapse into silence and her lips moved as if she were hearing voices, and when admitted to hospital it was found that she was definitely hallucinated. She was given 12 treatments with electronarcosis. After her 9th treatment she was able to take part in a hospital concert and after a period of convalescence she returned to work.

The following is a case of catatonic schizophrenia :—

Mrs H. was a patient of 51, who for ten years had been becoming rather hypochondriacal. Five months before being seen, she had become silent and depressed. She had talked of suicide, and razor blades were found secreted in her bed. Two weeks before being seen her condition had deteriorated. She said that she was going to be arrested and voices told her that she would be executed. She fell into a catatonic stupor, sitting without moving for hours on end, and if her arms were raised above her head, she kept them there indefinitely in a cataleptic manner. At times she became violent and in a state of catatonic excitement made several attacks on her husband and daughter, but could give no explanation for her behaviour.

The patient was given electric shocks without noticeable improvement, but with 18 treatments with electronarcosis she made a good recovery. Her voices left her. She was calm and rational and able to read serious books.

In the early part of treatment after she had improved, the treatment was discontinued, but she tended to relapse. Only when 10 treatments were given in twenty-one days did she become rational. She is now home and doing a full day's work, cooking, queueing, etc.

In this case as soon as the patient became mentally clear, she expressed a desire for psychotherapy and under great stress of emotion was able to discuss certain real problems which had worried her before the onset of her illness.

## THE RATIONALE OF THE TREATMENT

At the present time it is not quite clear why electric therapy of this kind effects an improvement in favourable cases. There has, however, been a theory from ancient times that a psychological shock might cure insanity. It is said that the priests of Apollo at Leucadia threw insane patients over the cliffs into the sea after attaching a number of living sea birds to them in order to break their fall. If the patient were subsequently rescued, it was hoped that his sanity would have returned.\* In the Middle Ages, certain monks who had ambitions as healers would hold an insane patient's head under water for as long as it took to say the Miserere (Thomas Willis, *De anima brutorum*), a period of time that would cause a high degree of anoxæmia, but not in most cases asphyxia! At Bethlem Asylum a hundred years ago, some patients were made to walk along a corridor in which a trap door had been placed in such a manner that the patient would fall into a pool of water below.

Such methods, however, produce a shock only at the conscious level. Since our patients do even better when they are anæsthetised before treatment, the shock, if we are to think in such terms, must be at the autonomic level, and not at the level of consciousness.

All that we can say with confidence is that for clinical improvement to occur, the patient must experience either a convulsion or else a coma such as that produced by insulin or electricity. Statistics show that shocks which do not produce a convulsion but only a *petit-mal*-like attack, do more harm than good.

At the present time we can only say that the treatment interferes with the autonomic and endocrine "sets" or patterns which accompany the morbid mental state. There is little doubt that the good effects are connected with changes in the autonomic centres around the third ventricle (Delay, 1946).

We are, however, only at the beginning. An immense amount of work still remains to be done in the fields of exact clinical observation, psychological measurements before and after treatment, electrophysiology, biochemistry and statistics, before we can be dogmatic regarding the *modus operandi* of these therapies.

## EXPERIENCES WITH ELECTRONARCOSIS

I should like now to summarise our findings in the first 50 cases in which we have used electronarcosis.

Some cases of severe agitation and mental tension which fail to respond to electro-shock, clear up rapidly with electronarcosis. Since in the past, those chronic cases which failed to respond to electro-shock went on to have a leucotomy, electronarcosis is likely to save many patients from the operation.

\* See Galt, *op. cit.*

With regard to the hazards connected with the treatment, we believe that since the current is controllable and as low as possible, there is a minimal risk of injuring the brain in any way, even although the current lasts longer than in electro-shock.

We have found that some patients who have been unable to discuss their mental conflicts before treatment, have been able after it to pour out an account of their difficulties, and so benefit from psychotherapy, which otherwise would have been impossible.

With patients under twenty years of age, however, we almost never give shock treatment, for in very young patients one can see the most alarming schizophrenic symptoms clear up with rest and psychotherapy, if we withhold physical treatment for a time.

Where we have a case of schizophrenia in the twenties, we generally advise insulin coma therapy. Where, however, this has not been feasible, we have given electronarcosis with the most satisfactory results and no ill after effects. The hallucinations rapidly disappear and twelve to eighteen treatments are often sufficient.

A curious fact, however, is that symptoms such as catalepsy and severe obsessions are sometimes intensified in the very early stages of treatment, only to disappear as the therapy proceeds.

After the patient's mental state has improved, it is sometimes found that certain physical diseases have disappeared, especially cases of chronic dermatitis.

In conclusion, I would say that it is always necessary to preserve a sense of proportion.

These treatments often do fail, and in any case provide only a minor part of the total psychiatric services of an area such as Hammersmith.

I thought, however, that it might be of interest to an audience such as this to hear of our efforts to lessen the hazards of these treatments, while at the same time increasing their effectiveness.

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## ŒSOPHAGEAL HIATUS HERNIA

By A. W. BRANWOOD, M.D., M.R.C.P.E.

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DIAPHRAGMATIC hernia had been recorded by Riverius in 1698, yet Morgagni, in 1769, was the first to describe herniation of the stomach through the œsophageal hiatus. In 1924, Abbott described small hernias involving the cardia of the stomach of the para-œsophageal type, and Morrison and Healey, in 1925, discussed the röntgen and clinical characteristics of these hernias. In the same year, Friedenwald and Feldman emphasised the special technical procedures necessary to demonstrate radiologically these small types of hernias. In 1926, Akerlund classified hiatus hernias into three types.

- I. Congenitally short œsophagus, producing a thoracic stomach.
- II. Para-œsophageal hernia. The lower œsophagus remains in its normal position, but a portion of the fundus of the stomach herniates through the hiatus alongside the œsophagus.
- III. Œsophago-gastric hernia. In this case, the lower end of the œsophagus and a portion of the fundus of the stomach prolapse through the hiatus.

Akerlund erroneously included congenital short œsophagus as a type of hiatus hernia. This is not so. It is the para-œsophageal hernia and the œsophago-gastric hernia, which are true hiatus hernias, and are encountered most frequently.

In spite of the reports by these workers, it is only in recent years that this lesion has been generally recognised as a cause of numerous, and often quite distressing, symptoms. Stapleton in a recent communication found this condition present in 4.6 per cent. of 522 selected cases. The frequency of this condition is illustrated by the following case records of 15 out of 300 patients (5 per cent.), who attended at a general out-patient department. All were out-patients, and although complaining of various symptoms, all were found to have an œsophageal hiatus hernia.

### CASE MATERIAL

#### (a) *Pain*

1. A woman, aged 66 years, complained of epigastric and retro-sternal pain of two years' duration. The pain was described as burning

in character, and occurred immediately after eating and on lying down in bed. An X-ray demonstrated an œsophageal hiatus hernia.

2. A man, aged 57 years, had suffered from retrosternal pain and heartburn for four years. Both symptoms were brought on by lying down after meals, and on some occasions severe exertion caused the pain. The pain has been likened to a sensation of pressure and was relieved by assuming the upright posture, or by ceasing to exert himself. The blood pressure was 138/88, there was no clinical evidence of heart disease, and an electrocardiogram taken before and after exercise showed no abnormalities. X-ray examination showed a hernia of the stomach through the œsophageal hiatus.

3. A woman, aged 52 years, stated that for three years she had had retrosternal pain, heartburn and flatulence. The pain was described as burning, and on occasions, crushing in character. It would be brought on by hurried meals, drinking hot liquids, stooping, straining at stool or by a fit of coughing. A hiatus hernia with a degree of œsophageal spasm was detected by radiological examination.

4. A man, aged 59 years, had complained of a burning sensation behind the sternum, which was caused by hurried meals or by exertion ; in either case the pain radiated up to his left shoulder and down the medial side of his left arm as far as the elbow. An attack of pain could also be initiated by a sudden twist or turn of the body. No abnormalities were detected in his cardio-vascular system, but the electrocardiogram showed left axis deviation. There was an œsophageal hiatus hernia present on X-ray examination.

5. A man, aged 43 years, suffered from a crushing retrosternal pain and gastric flatulence for eighteen months. The pain followed the intake of food but could also be caused by straining at stool or lifting any heavy object. The pain radiated up into the jaw and down the medial aspect of the left arm as far as the wrist and hand. Clinical examination of the cardiovascular system revealed no abnormalities ; the electrocardiograms, before and after exercise, were normal. An X-ray showed a hiatus hernia.

6. A woman, aged 60 years, had complained of epigastric pain, lasting about an hour, occurring immediately after the intake of food, for a period of two years. The pain was much worse when she was recumbent, and at times it was situated behind the sternum. Any exertion after food would make the pain worse, and on these occasions the pain was experienced in the neck and left shoulder. Examination of the heart was negative, apart from a degree of left axis deviation. An œsophageal hiatus hernia was revealed by X-ray examination.

7. A woman, aged 52 years, had for the past eighteen months experienced a burning epigastric and retrosternal pain on lying down in bed. The pain was relieved by sitting upright. During the day she complained of heartburn and mild attacks of indigestion. An œsophageal hiatus hernia was seen on radiological examination.



(b) *Dysphagia*

8. A woman, aged 68 years, had suffered from dysphagia for two months. This was only present after eating solid, hot or very dry food. It had not become worse. An X-ray showed a small œsophageal hiatus hernia.

9. A man, aged 50 years, had experienced dysphagia following the ingestion of morsels of dry food or very hot liquid. He also experienced attacks of heartburn and a sensation of constriction in his chest on stooping. A hiatus hernia was detected on radiological examination.

10. A woman, aged 46 years, had suffered from transient attacks of dysphagia associated with gastric flatulence over a period of two and a half years. Radiological examination showed a large hiatus hernia.

(c) *Heartburn*

11. A woman, aged 60 years, had complained of heartburn for six months. This symptom occurred within fifteen minutes of the intake of food and on occasions wakened her from sleep. It was relieved by alkaline powders. No tenderness was elicited on palpation of the epigastrium, but a barium meal showed a hiatus hernia with a degree of œsophageal spasm.

12. A woman, aged 55 years, had symptoms of "heartburn and indigestion" for many years. Recently this complaint had occurred more frequently, was more severe and usually brought on by lying down. The symptoms were relieved by alkalis. An X-ray showed an œsophageal hiatus hernia.

(d) *Flatulence*

13. A woman, aged 48 years, had complained of gastric flatulence for many years. Recently it had become worse and had prevented her from sleeping. On examination tenderness was elicited in the right hypochondrium, and a straight X-ray and opacol examination showed a non-functioning gall bladder in which was a single calculus. Cholecystectomy was performed, but the patient reported back in six months' time stating that the flatulence was no better. A barium meal was given and a large hiatus hernia was seen.

(e) *Vomiting*

14. A woman, aged 51 years, had had repeated attacks of vomiting for a period of twelve months. These used to occur immediately after the intake of food, were present for some days, but would then disappear for two to three weeks only to return. The patient knew of no cause for these attacks. An X-ray showed a hiatus hernia.

(f) *Hæmatemesis*

15. A woman, aged 30 years, six months' pregnant, complained of vomiting a small quantity of blood; this was followed by slight



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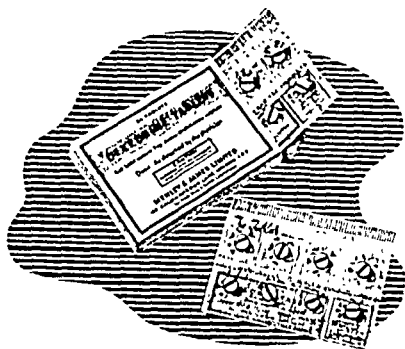
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dysphagia and associated heartburn for one week. X-ray examination revealed a hiatus hernia.

Twelve of these 15 patients were obese.

### ÆTIOLOGY

Weakness of a muscular wall, and increased intra-mural pressure are the main accepted causes of hernia.

Congenital weakness of the diaphragm or an unduly wide œsophageal opening may be present in these patients and predispose to herniation through the hiatus. These hernias usually give no symptoms until later in life, the average age of the patients in this series was 55·8 years; therefore it is suggested that hiatus hernias may not develop until later life.

The loss of elastic tissue, with replacement by adipose tissue, which is known to occur in elderly patients, may cause relaxation of the diaphragm and hence enlargement or weakening of the œsophageal hiatus. Schatzki states that small hiatus hernias may be physiological in later life due to muscular relaxation and decreased elasticity of the diaphragm. This hypothesis is supported, for, 80 per cent. of the patients in this series were obese and most of the cases described in the literature were, or had been, overweight.

Most workers state that increased abdominal pressure aggravates the symptoms of the condition, and it is feasible to suggest that increased pressure may have played a part in the causation of this lesion. The wearing of tight corsets, especially by obese women, may be one factor in the development and explains the large number of cases seen in the female sex. In this series 76 per cent. were women.

The associated increased abdominal pressure of pregnancy and parturition may be another factor in explaining this high sex incidence. In this series, a hiatus hernia, the only presenting symptom of which was hæmatemesis, was demonstrated in a pregnant woman. Other conditions causing increased intra-abdominal pressure and which have been noted in cases of hiatus hernia are:—sudden trauma to the chest and abdomen, mega-colon, ascites, chronic constipation with straining at stool, prolonged spasms of coughing or vomiting and severe physical exertion.

Von Bergmann, in 1932, suggested that reflex contraction of the longitudinal muscle fibres of the œsophagus, perhaps due to vagal stimulation and produced by cholecystitis, may cause hiatus hernia. The well-known sex incidence of cholecystitis, and the large number of hiatus hernias present in female patients, may be more than just coincidence. The significance of this, however, could only be ascertained by assessing the function of the gall bladder in these cases.

Held and Goldbloom state that the cause of hiatus hernia and the thoracic stomach of Le Wald, Fineman and Conner is due to the presence of a large hiatus. This produces the hernia, with later

secondary shortening of the œsophagus due to vagal irritation in the hernia. Held and Goldbloom have demonstrated contraction and shortening of the œsophagus caused by vagal irritation. This shortening of the œsophagus may be the explanation for the fixation of these hernias above the diaphragm.

The majority of the patients with a hiatus hernia were obese and of the "gall bladder type"; it would be intriguing to suggest an association between disease of the gall bladder and the ætiology of hiatus hernia. One patient in this series with a hiatus hernia, but no symptoms of cholecystitis, had tenderness over the gall bladder on examination, and was found to have a non-functioning gall bladder and gall stones.

### CLINICAL FEATURES

*Pain.*—This was the most frequent complaint. It was the presenting symptom in 46·7 per cent. of the patients in this series. It is commonly situated behind the sternum or in the epigastrium. In this series 20 per cent. of the total cases, or 43 per cent. of the patients complaining of pain, described the pain as radiating up into the neck, left shoulder and down the left arm. This symptom may therefore simulate the pain of angina pectoris. This referred pain is perhaps due to communications between the œsophageal and cardiac plexuses. Lesions of the œsophagus could therefore cause pain, which is referred to the same regions as that from the heart. Distension of the hernial pouch may displace the heart and so stimulate the cardiac nerves and thus produce the typical referred pain. The hiatus hernia may also irritate the sensory endings of the phrenic nerve and cause pain to be felt in the distribution of C3 and C4 and sometimes C5.

The pain occurs immediately after meals and when lying down. The occurrence of pain of this nature in an elderly obese woman should suggest the possibility of a hiatus hernia. The pain may arise during exercise, straining at stool, coughing or by a sudden twist to the trunk. The symptom is relieved by assuming the upright posture, by the administration of alkalis or anti-spasmodics.

The primary causes of the pain are probably irritation of the lower end of the œsophagus, spasm of the gastric musculature or distension of the pouch.

This may occur after a meal or when the other viscera press upon the stomach when the patient is recumbent, and force the gastric pouch further into the hiatus. The hernial pouch may be compressed or irritated by movement of the diaphragm during exercise or when straining.

*Dysphagia.*—Difficulty in swallowing was the next most frequent symptom. It is probably due to ulceration or inflammation of the lower end of the œsophagus. It was the main complaint of 20 per cent. of these patients. It was usually brought on by hurried meals, swallowing large morsels of rough or very dry food or hot liquid.

The dysphagia does not usually progress and can be relieved by alkalis or anti-spasmodics.

*Heartburn.*—This symptom occurred in 13·3 per cent. of patients. The explanation is probably irritation and spasm of the lower end of the œsophagus.

*Flatulence and Vomiting.*—Both complaints were present in 6·6 per cent. of cases. The flatulence was most probably caused by the swallowing of air. The vomiting was produced by over-distension of the hernia or irritation of the fundus of the stomach.

*Hæmatemesis.*—This symptom has been reported by some investigators. Morein described hæmatemesis in 21 per cent., melæna in 17 per cent. and anæmia in 23 per cent. of his cases. Hæmatemesis was the only symptom of one patient in this series. The anæmia, melæna or hæmatemesis may be due to:—ulceration in the hernial pouch as described by Truesdale, Harrington, Hurst and Schilling; constriction of the pouch interfering with its normal blood supply; erosions of the herniated portion; œsophagitis or concomitant gastric or duodenal ulcer.

*Radiological Examination.*—A barium meal is essential in the diagnosis of hiatus hernia. It is also useful to determine which type of hernia is present or to demonstrate the presence of any complication. An X-ray should also be taken of the heart and gall bladder.

The patient should be examined when lying down and when erect, to determine whether or not the stomach remains above or returns below the diaphragm. The pouch returning below the diaphragm when the patient is upright indicates the presence of a hiatus hernia of the sliding type. The Trendelenburg position is also useful to detect this sliding type of hernia, and has been used for the purpose by Morrison since 1925. Deep breathing while in the recumbent position may demonstrate the presence of a small hernia as was first emphasised by Friedenwald and Feldman. Heavy compression of the abdomen, or the method of Schatzki of distending the colon with air have been condemned by Hurst as too strenuous for elderly patients.

*Œsophagoscopy.*—This examination will differentiate between a true hiatus hernia and a congenital short œsophagus even better than radiological investigation. It will confirm the presence of an œsophageal ulcer or œsophagitis, and may reveal a carcinoma of the lower end of the œsophagus. This latter condition may have been masked by the hernia.

#### DIFFERENTIAL DIAGNOSIS

1. *Gastric and duodenal ulcer* may have symptoms similar to these of hiatus hernia. The periodicity of the pain, said to be characteristic of these conditions, need not be present, or the symptoms of a hiatus hernia may be periodic. Anæmia may be present in both cases. X-ray examination or gastroscopy are the only means of differentiation.

2. *Gastric or œsophageal carcinoma* may give rise to symptoms

difficult to distinguish from those of hiatus hernia. Here again, radiological examination, œsophagoscopy or gastroscopy are all important.

3. *Cholecystitis* may be present at the same time and indeed, according to some workers, may have caused the hernia. Symptoms of cholecystitis may mimic those of hiatus hernia. A straight X-ray of the gall bladder followed by an opacol examination and a barium meal will determine the presence of both lesions.

4. *Angina Pectoris*.—The differential diagnosis between hiatus hernia and angina pectoris may be extremely difficult. Points to be considered are :—

- I. The sex incidence. Angina pectoris is more common in men while hiatus hernia is met with most frequently in women. Both conditions, however, may occur in either sex.
- II. The presence of the same type of pain following exertion as occurs immediately after eating—the pain being relieved by standing upright—is very suggestive of a hiatus hernia.
- III. The pain is often described as burning in character in the case of hiatus hernia, but may, in some instances, be of a crushing nature, similar to angina of effort.
- IV. Examination of the heart may reveal enlargement in the case of angina pectoris ; the heart may, however, be displaced to the left by a very large hiatus hernia.
- V. Hypertension will probably be present in the patient with coronary vessel disease, but is quite likely to be present also in the elderly obese female who suffers from a hiatus hernia.
- VI. The electrocardiogram will show changes in the S.T. segment and perhaps left axis deviation in the patients suffering from angina pectoris. If the patient is fit, these changes will be more pronounced following an exercise tolerance test. In cases of hiatus hernia the electrocardiogram may show left axis deviation due to displacement of the heart by the hernia. Two of the three cases of hiatus hernia in this series, in which the symptoms simulated anginal pain, showed left axis deviation on electrocardiographic examination, although the blood pressure was not elevated and there was no other evidence of cardiovascular disease. When an exercise tolerance test is performed, the patient with hiatus hernia may complain of pain, but the electrocardiogram taken immediately afterwards should show no gross abnormalities. An electrocardiogram taken after air insufflation of the stomach and hernial pouch may demonstrate further increase in the left axis deviation with perhaps slight changes in the S.T. segment.

VII. A barium swallow and meal will demonstrate the hiatus hernia and thus confirm the diagnosis.

VIII. Amyl nitrite may relieve the pain in both conditions and is therefore of no diagnostic aid.

5. *Other Œsophageal Lesions.*—Œsophagitis and peptic ulcer of the œsophagus can only be diagnosed by X-ray examination or œsophagoscopy.

### TREATMENT

The patient, if obese, should be given a diet to reduce her weight. If the symptoms are severe, then the dietary treatment should be similar to that for peptic ulcer, and the weight reduced at some later date. Antacids and anti-spasmodics should be given during the day and phenobarbitone administered at night. Sleeping in the upright position or semi-recumbent posture gives relief from the distressing nocturnal symptoms. If an attack of pain should occur when in bed, assuming the upright posture or walking about the room usually gives immediate relief.

Causes of increased intra-abdominal pressure such as exercise, stooping or straining should be avoided. Constipation should be adequately treated, and abdominal supports or corsets must not be worn.

Surgical treatment is rarely required. If the hernia occurs in a young patient, and the symptoms are distressing, or if in an elderly patient the symptoms are severe and do not respond to medical treatment, which is unusual, then the operation of phrenicotomy, recommended by Harrington, may be performed. This procedure alone may prevent spasm of the diaphragm and relieve the symptoms. Following the phrenicotomy the hernial opening can be sutured around the lower end of the œsophagus above the hernial pouch. Von Bergmann and Held and Goldbloom have suggested that vagal irritation produces spasm of the longitudinal muscle of the œsophagus and is perhaps a predisposing factor in the ætiology of hiatus hernia. They also explain the fixation of these hernias above the diaphragm on this basis. If this is so then vagotomy may relieve the symptoms and be the operation of choice.

### SUMMARY

Fifteen cases of œsophageal hiatus hernia, presenting varied symptoms, are described. The ætiology, symptomatology, diagnosis and treatment are discussed.

I wish to thank Professor D. M. Lyon for the use of the case material and for his help in the compilation of this paper.



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*Photo by*

JOHN FRASER

*Moffat, Edinburgh*

# OBITUARY

## SIR JOHN FRASER

At the age of forty Sir John Fraser was selected by His Majesty The King as Regius Professor of Clinical Surgery of Edinburgh University.

His career up to then had been one of evolution from success to success.

He was born in Tain, Ross-shire, where he received his early education. His progress during his medical course in Edinburgh was creditable, but in no way outstanding. In a race for distinction he always was to be found as a member of the fast pack, running in an effortless style that suggested he was holding his strength in reserve, and thus he ultimately graduated with Honours with a creditable place in the foremost pack.

From the early days of his post-graduate career his sterling worth was revealed. As Annandale's last Resident he got an introduction to practical surgery and from the first showed that herein was his career to be marked out. His associationship with Sir Harold Stiles in the Children's Hospital and Chalmers Hospital and in private practice were further stepping-stones in his surgical career.

When the first world war broke out he, as a member of the Special Reserve of Officers of the Royal Army Medical Corps, was mobilised and proceeded to France where he saw service, and for his courage in action was awarded the Military Cross. His work as a surgeon in the Field and his observations on the treatment of wounds and of shock soon gained for him an outstanding position among the young medical men on service, so that by his writings he came to be recognised as an outstanding young man in the world of international surgery, and with this creditable record he returned to civilian practice in Edinburgh to resume his research work in the Royal College of Physicians' Laboratory which had been interrupted by the outbreak of war. In the pre-war years, when this research was undertaken, active operative treatment was being widely practised in the treatment of surgical tuberculosis. By utilising the material thus available, Fraser carried out a piece of research which had a widespread repercussion, wherein he and his co-workers demonstrated that in the majority of cases of surgical tuberculosis the infection was due to the tubercle bacillus of bovine origin, disproving Koch's opinion to the contrary. On this work was largely founded the institution of tuberculin-tested dairy herds and the campaign for clean milk.

In 1914 he published a book that is now a classic entitled *Tuberculosis in the Bones and Joints in Children*, a book which revealed the author to be an industrious and able observer and also one in possession of a charming literary style.

On his return to Edinburgh he was appointed Surgeon to the Royal Hospital for Sick Children and shortly thereafter an Assistant Surgeon to the Royal Infirmary of Edinburgh, and in associationship with the late Sir David Wilkie he lectured on surgery in the Surgeons' Hall, a combination of ability that naturally attracted large classes of University and College students. This partnership was broken when Wilkie was appointed Professor of Surgery to the University and later when Fraser himself became Regius Professor of Clinical Surgery.

National and international distinctions were now conferred upon him frequently.

As Surgeon to His Majesty The King he was knighted.

He visited by invitation the United States of America, Canada and Australia on several occasions, and was awarded the Honorary Fellowship of their Colleges.

In 1943 he was made a Baronet.

In 1944 he became Vice-Chancellor and Principal of Edinburgh University. His short tenure of this post was handicapped by two critical illnesses. During it, however, he earned for himself a further reputation by the able manner in which he discharged his duties and particularly endeared himself to the students whose interests were ever first-thought in his mind.

In his day John Fraser received many honours and was awarded many distinctions. The one, however, he treasured most was the award of the Freedom of the Burgh of Tain, a testimony to a son of the pride the townsfolk had in his distinguished career. At the same time, it was treasured by that son as a grateful acknowledgment of his good fortune in having been brought up in this Scottish country town during those early years when the character of a youth is moulded. He then lived in a community where true democracy is practised and personal worth is the real test of the social pre-eminence, and in a community whose standards of judgment of their sons' careers has a similar basis. From this source into this growing youth there was also instilled that love of humanity, kindly tolerant sympathy and a humility and industry which were so manifest in John Fraser's later life. He was a great surgeon, pre-eminent and expert in all its branches, a great teacher, a sound scientific observer and a wise Principal, but above all a great gentleman.

H. W.

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## NEW BOOKS

*Essentials of Clinical Proctology.* By MANUEL G. SPIESMAN. Pp. 238. London: William Heinemann (Medical Books) Ltd. 1946. Price 21s.

This book is a monograph published by Dr Spiesman, and based on his lectures to undergraduates and post-graduates at the Cook County Hospital Rectal Clinic in Chicago. While the book covers a considerable amount of useful ground and is quite well laid out, it is rather full for the undergraduate and does not go into sufficient detail for the post-graduate. Dr Spiesman's practice in various ano-rectal conditions is described in considerable detail and the book is well illustrated. There is, however, a great deal of unnecessary repetition both in the text and also in the explanations of the illustrations. Certain conditions which would normally be perhaps without the ano-rectum, such as the treatment of pilonidal cyst, are discussed. There is an excellent "proctologic reference book list" at the end.

*A Contribution to the Knowledge of the Influences of Gonadotropic and Sex Hormones on the Gonads of Rats.* By J. H. GAARENSTROOM and S. E. DE JONGH. Pp. 164, with 20 illustrations. Distributors: Cleaver-Hume Press. 1946. Price 16s. net.

The authors of this monograph are to be congratulated on their courage and pertinacity in carrying on their scientific work under very difficult conditions during the German occupation of Holland. As the title suggests, the effect of the gonadotrophic hormone on the gonads of rats was carefully investigated and the results correlated. One of the objects of the investigation was to produce biological proof of the independent existence of two gonadotrophic hormones in one and the same species. The authors not only produce evidence which appears to substantiate their hypothesis, but indicate that there is a much closer inter-relationship between the gonadotrophic and sex hormones than was considered formerly. The investigations suggest that the sex hormones often act as a link between the gonadotrophic hormones and certain morphological processes in the gonads. They employ a neutral descriptive nomenclature for the two gonadotrophic hormones, namely, Gi—interstitium factor, and Ge—epithelium factor.

Although the monograph deals for the most part with experimental work, it is of absorbing interest and should be read by all interested in sex endocrinology.

*Experiences with Folic Acid.* By TOM D. SPIES. Pp. 110, with 4 coloured plates. Chicago. (London: H. K. Lewis & Co.). 1947. Price 21s. net. \$3.75.

A summary of the work leading to the successful therapeutic use of synthetic folic acid is followed by an account of the formidable list of investigations carried out by Spies and his co-workers on each patient. Folic acid was effective in the treatment of megaloblastic anæmia of various types, and in what is described as nutritional leucopenia. It produced definite hæmatological and clinical improvement in cases of sprue.

The danger of subacute combined degeneration of the cord occurring when folic acid is used alone in the routine treatment of pernicious anæmia is stressed. There is a brief discussion of the part played by folic acid and its conjugates in hæmopoiesis. As yet no definite conclusion has been reached as to its mode of action.

*Child Health.* (The Practitioner Handbooks.) Edited by ALAN MONCREIFF, M.D., F.R.C.P., and WILLIAM A. R. THOMSON, M.D. Pp. 254. London: Eyre & Spottiswoode Ltd. 1947. Price 14s. net.

This volume clearly unfolds in its twenty-two chapters the management of the disorders which are likely to become the care of the general practitioner under the National Health Service, necessitating on his part a wide knowledge of the services available and how they may be utilised to the best advantage.



A detailed description of the organisation and administration of Child Health Services and the facilities available for the care and education of the child at different ages is set out. The common problems of infant feeding and hygiene, of the toddler, the school child and the care of the physically handicapped, mental and problem child are dealt with.

This book is full of helpful advice and information for those who have the supervision of the upbringing of children.

*Recent Advances in Clinical Pathology.* Edited by S. C. DYKES, D.M., F.R.C.P. Pp. xii+468, with 34 plates and 19 figures. London: J. & A. Churchill. 1947. Price 25s.

This new volume, issued under the auspices of the European Association of Clinical Pathologists, is a valuable addition to the series of Recent Advances.

The editor has secured the services of about forty collaborators, each an expert in his own department. The book is divided into four sections which deal respectively with Bacteriology, Biochemistry, Hæmatology and Histology, and covers a wide range of subjects. The information collected has been well chosen and is authoritative and reliable.

The book is excellently produced and well illustrated and it should become a popular member of this well-known series.

*The Psychology of the Unwanted Child.* By AGATHA M. BOWLEY, PH.D. Pp. xi+112. Edinburgh: E. & S. Livingstone. 1947. Price 6s. net.

Miss Bowley has tried to help matrons, wardens, housemothers, and all those who are responsible for the care of children removed from their own homes, to understand something of the child's point of view, his feelings and his difficulties. A clear, simple and readable book results. We commend particularly her advocacy of the value, under proper conditions, of institutions in the care of problem children.

*The Practice of Mental Nursing.* By MAY HOULISTON, R.G.N., R.M.N., R.F.N. Pp. xi+164. Edinburgh: E. & S. Livingstone. 1947. Price 7s. 6d. net.

Miss Houlston has designed this book as a brief elementary introduction to the practice of mental nursing, including an attenuated account of normal psychology and of psychiatry, in the belief that there is no other such introductory book for use in preliminary training schools. There are already a number of books on mental nursing, and we still think that the *Handbook of the Royal Medico-Psychological Association* is the most suitable manual for nurses in training and that Sister-Tutors should introduce and guide their probationers to the subject.

*The Psychology of Women.* Vol. II: *Motherhood.* By HELENE DEUTSCH, M.D. Pp. vi+436. London: William Heinemann (Medical Books) Ltd. 1947. Price 25s. net.

This volume is an excellent counterpart of the previous volume, and maintains its high standard. It deals with the psychologic life of the normal woman, and while the interpretations are based on psycho-analytic doctrine, yet the picture is never overdrawn and the deductions are reasonable. The psychosomatic interdependence of the processes involved is always kept fully in mind, and the conditions described are related to the social and economic circumstances. This book is not only of intense interest to psychiatrists, but it can be recommended cordially to all practising obstetricians and gynecologists.

*Elements of Surgery.* By FAUSET WELSH, B.SC., M.B., F.R.C.S.(ENG.). Pp. viii+83. London: Oxford University Press. 1947. Price 7s. 6d. net.

This book is the outcome of lectures given to nurses. It is hoped that it might be welcomed by medical students as well. The text is clear and up-to-date, but it suffers from compression and lack of illustrations—both dangerous in a "primer." It covers the syllabus for the S.R.N.

## NEW EDITIONS

*Insect Pests.* By WM. CLUNIE HARVEY, M.D., D.P.H., M.R.SAN.I., and HARRY HILL, F.R.SAN.I., F.S.I.A., A.M.I.S.E. Second Edition. Pp. xi+374, with 27 illustrations. London: H. K. Lewis & Co. Ltd. Price 14s. net.

In this compact volume is contained a mass of information on insect extermination, on a small scale, as a public health measure and at public installations.

The instructions are clearly for the medical officer of health or trained sanitary inspector, as many of the methods would be dangerous in the hands of amateurs.

The authors open with a description of the appearance and habits of those members of the insect family calling for destruction whether as disease carriers, or as being destructive or merely noxious.

Chapters are devoted to house construction with a view to avoiding refuges for insects, to detailed descriptions of methods of extermination, and of municipal installations. The reader is furnished with a summary of the legal authority under which he may act in the interest of public health. Finally a chapter is allotted to the disinfection of ships.

In brief, those engaged in this branch of sanitary work, will find in this book remarkably concise, full and comprehensive instructions.

*The Principles and Practice of Obstetrics.* By JOSEPH B. DE LEE and J. P. GREENHILL. Ninth Edition. Pp. x+1011, with 860 illustrations. Philadelphia and London: W. B. Saunders Company. 1947. Price 50s.

Although retaining the general characteristics of previous editions, this one has been practically rewritten by Dr J. P. Greenhill. Only in a few instances has the help of experts been called for in the presentations of special subjects. New chapters appear on "Minor Disturbances of Pregnancy," "Premature Labour, Prolonged Pregnancy or Post-maturity and Missed Labour," "Fœtal Erythroblastosis," "Care of Premature Babies" and "Circumcision." Throughout every effort has been made to incorporate the latest views and at the end of each chapter is to be found a bibliography containing the original references for every name mentioned in the text.

The numerous and excellent drawings, diagrams and photographs are beautifully reproduced and illustrate the text in a way that must be the envy of many a British author.

There is a vast store of information to be found in this book but its appreciation requires a considerable practical experience of obstetrics, so that the volume is essentially for the consultant rather than the occasional obstetrician. It constantly stimulates and provides for a critical evaluation of the methods described and views expressed. For example it must be seldom that the "key in the lock" method of rotating a persistent occipito-posterior position by forceps, described and illustrated in detail, is the method of election. This contrasts with the opinion that Credé's manipulation to expel the placenta is dangerous and should not be used, rather should the placenta be removed manually forthwith in the presence of hæmorrhage. Yet such comes from the school where the mottoes on the delivery theatres are *Primum non Nocere* and *Non Vi sed Arte*, and must therefore have been carefully assessed before publication.

Without doubt this edition makes a fitting memorial to the late Dr Joseph B. de Lee.

*A Text-book of Midwifery.* By WILFRED SHAW, M.D., F.R.C.S., F.R.C.O.G. Second Edition. Pp. 649. London: J. & A. Churchill Ltd. 1947. Price 21s.

The second edition of Mr Shaw's text-book contains new matter including a section on erythroblastosis and the Rhesus factor. It would seem that the obstetrician is destined to teach the undergraduate the fundamentals of this subject, and this

part of the book might well be expanded. For instance, the student should be informed of the meaning of the conventional symbols Rh and rh, and a brief synopsis of Fisher's nomenclature included. The chapter on the toxæmias of pregnancy must surely be rewritten in a future edition. The term "albuminuria of pregnancy" is now meaningless, glomerulo-nephritis is a relatively rare complication of pregnancy; cardiovascular hypertension, which is not considered separately, is extremely common. The major portion of this book contains sound teaching, and the section on accidental hæmorrhage is one which the reviewer has long admired. It remains an excellent text-book for the undergraduate.

## BOOKS RECEIVED

- BALLENGER, HOWARD CHARLES, M.D., F.A.C.S. A Manual of Otolaryngology, Rhinology and Laryngology. Third Edition (*Henry Kimpton, London*) 22s. 6d. net.
- BEAUMONT, G. E., M.A., D.M.(OXON.), F.R.C.P., D.P.H.(LOND.). Medicine: Essentials for Practitioners and Students. Fifth Edition. (*J. & A. Churchill Ltd., London*) 30s.
- BREEN, GERALD E., M.D., B.CH. (N.U.I. DUB.), D.P.H., D.O.M.S. (R.C.P. LOND., R.C.S. ENG.). Essentials of Fevers. Second Edition. (*E. & S. Livingstone Ltd., Edinburgh*) 15s. net.
- BURCH, GEORGE E., M.D., F.A.C.P., and REASER, PAUL, M.D. A Primer of Cardiology. (*Henry Kimpton, London*) 22s. 6d. net.
- Edited by DALEY, RAYMOND, M.A., M.D. (CAMB.), M.R.C.P., and MILLER, HENRY G., M.D. (DURIHAM), M.R.C.P., D.P.M. Progress in Clinical Medicine. (*J. & A. Churchill Ltd., London*) 21s.
- DOGGART, JAMES HAMILTON, M.A., M.D. (CANTAB.), F.R.C.S. ENG. Children's Eye Nursing. (*Henry Kimpton, London*) 8s. 6d. net.
- DONALDSON, J. K., B.S., M.D., F.A.C.S. (LT.-COL. A.U.S.). Surgical Disorders of the Chest: Diagnosis and Treatment. Second Edition. (*Henry Kimpton, London*) 42s. net.
- FORD, ROSA, M.B. (LOND.), D.O. (OXON.). Chronic Ill-Health: Relieved by Drainage of the Para-Nasal Sinuses. (*Henry Kimpton, London*) 6s. net.
- By the late GIFFORD, SANFORD R., M.D., F.A.C.S. Revised by VAIL, DERRICK, M.D., D.O. (OXON.), F.A.C.S. A Handbook of Ocular Therapeutics. Fourth Edition. (*Henry Kimpton, London*) 25s. net.
- GOLDBERGER, EMANUEL, B.S., M.D. Unipolar Lead Electrocardiography. (*Henry Kimpton, London*) 20s. net.
- HALE-WHITE, WILLIAM, K.B.E., M.D. (LOND.), M.D. (DUBLIN), LL.D. (EDIN.). Revised by DOUTHWAITE, A. H., M.D., F.R.C.P. Materia Medica: Pharmacy, Pharmacology and Therapeutics. Twenty-seventh Edition. (*J. & A. Churchill Ltd., London*) 15s.
- Edited by HANDFIELD-JONES, R. M., M.C., M.S., F.R.C.S., and PORRITT, A. E., C.B.E., M.A., M.CH., F.R.C.S. The Essentials of Modern Surgery. Third Edition. (*E. & S. Livingstone Ltd., London*) 50s. net.
- HARRIS, D. T., M.D., D.SC., F.INST.P. Practical Histology for Medical Students. Fourth Edition. (*H. K. Lewis & Co. Ltd., London*) 12s. 6d. net.
- LEWIN, PHILIP, M.D., F.A.C.S. The Foot and Ankle. Third Edition. (*Henry Kimpton, London*) 55s. net.
- MARTIN, C. R. A. Practical Food Inspection. Vol. I.: Meat Inspection. Third Edition. (*H. K. Lewis & Co. Ltd., London*) 18s. net.
- RADCLIFFE, WALTER. The Secret Instrument (The Birth of the Midwifery Forceps). (*William Heinemann (Medical Books) Ltd., London*) 10s. 6d. net.
- SELLING, LOWELL S., M.D., PH.D., D.P.H., F.A.C.P. Synopsis of Neuropsychiatry. Second Edition. (*Henry Kimpton, London*) 32s. 6d. net.
- The Medical Annual, 1947. (*John Wright & Sons Ltd., Bristol*) 25s.
- THORELL, BO. Studies on the Formation of Cellular Substances during Blood Cell Production. (*Henry Kimpton, London*) 12s. net.
- TREDGOLD, A. F., M.D., F.R.C.P., F.R.S. (EDIN.). A Text-Book of Mental Deficiency (Amentia). Seventh Edition. (*Baillière, Tindall & Cox, London*) 30s. net.
- WILLIS, R. A., D.SC., M.D., F.R.C.P. Pathology of Tumours. (*Butterworth & Co. (Publishers) Ltd., London*) 63s.
- WINTERTON, W. R., M.B., B.CH. (CAMB.), F.R.C.S. (ENG.), M.R.C.O.G. Aids to Gynæcology. Tenth Edition. (*Baillière, Tindall & Cox, London*) 5s. net.

# Edinburgh Medical Journal

*February 1948*

## HEART FAILURE OF PULMONARY ORIGIN \*

By JOHN McMICHAEL, M.D., F.R.C.P. Edin., F.R.C.P. Lond.

Professor of Medicine, University of London ; Director, Department  
of Medicine, Post-graduate Medical School of London

### INTRODUCTION

It is always a difficult task to lecture for an hour on a subject which has been the centre of one's interest, thought and research for a period of many years. While one would wish to deal with the subject completely and in all its aspects, one can only bring out the high lights as they appear to an active worker in the field. So long as research is proceeding energetically, the views expressed to-day may be considerably modified to-morrow. In trying to organise ideas on a rapidly changing subject, each investigator is inclined to emphasise certain facts at the expense or detriment of others. New light is likely to come rapidly in this subject from the steadily accelerating use of new and more accurate methods for the combined study of the heart pressures and output on the one hand, and pulmonary function on the other, most brilliantly exemplified to-day by the work of Cournand and Richards and their co-workers in New York. I would therefore ask you to regard what I have to say as an interim report on progress rather than a new chapter of a static textbook.

In this lecture I shall deal only with those conditions of heart failure which result from diseases primarily affecting the lungs or pulmonary arteries. Before going on to this subject, however, I should mention that the commonest cause of right heart failure is left heart failure. Attacks of left ventricular failure are nearly always accompanied by venous congestion in the systemic circulation, and in many cases of mitral stenosis the right ventricle is very grossly affected. Bloomfield and his colleagues (1946) have recently shown that, in severe mitral stenosis with heart failure, the systolic pressure in the pulmonary artery may rise to over 100 mm. mercury, but with recovery from the attack of failure it subsides to about 60 mm. mercury. This pressure is considerably above the normal upper normal limit of 30 mm. Hg. for the pulmonary systolic pressure. Why some cases of mitral stenosis develop an accompanying pulmonary hypertension

\* A Honyman Gillespie Lecture given in the Royal Infirmary, 23rd October 1947.

and others do not, is a matter requiring further study. In uncomplicated essential hypertension, without heart failure the pressure in the pulmonary artery is normal, but when heart failure develops it rises considerably above normal. Many of the varieties of congenital heart disease also cause right heart strain but these also are beyond the scope of this talk.

## ETIOLOGY AND INCIDENCE OF PULMONARY HEART DISEASE

Right heart strain consequent upon primary disease in the lungs, particularly emphysema, has long been recognised by the pathologist who sees at post-mortem the hypertrophied and dilated right ventricle and the frequently atheromatous pulmonary artery, the latter change being ascribed to an accompanying pulmonary hypertension. In spite of the frequency of chronic bronchitis and emphysema cardiologists have often given it as their opinion that the disease is rare. Thus White and Jones (1928) saw only 21 cases of emphysema heart in 2314 cases of organic heart disease. Parkinson and Hoyle (1937) only found evidence of right ventricular hypertrophy on radiological examination in 18 out of 80 cases of emphysema. Scott and Garvin (1941), on the other hand, found the right ventricle more than 5 mm. thick at post-mortem in 80 per cent. of 48 cases of emphysema of varied etiology: most pathologists would endorse that finding. There are several reasons for this discrepancy of opinion: (1) Chronic bronchitis is a condition which is not seen nearly so much in teaching hospitals as in municipal hospitals, as these patients are frequently labelled "chronics"; (2) The primary disease is often present for many years without any obvious cardiovascular manifestations, and it is only in the late stages that these develop in a form likely to compel the interested attention of the cardiologist; (3) The development of right heart strain in these patients is not dramatic and in the early stages it is still a difficult matter to decide whether breathlessness is due to the pulmonary or cardiac component of the disease process. The absence of murmurs and other striking physical signs are further factors tending to divert these cases away from the teaching hospital.

There is a widespread impression that chronic bronchitis is commoner in males than females, and this is confirmed by my own experience. In the last eight years I have had 134 cases of chronic bronchitis under my personal care, and of these only 24 have been women, a sex incidence of about 9 males to 2 females. When one adds the occupational hazards of silicosis in the male population, and assuming the nearly equal sex incidence of the other and rarer causes of chronic cor pulmonale, the great preponderance in the male becomes obvious.

In addition to the chronic form of cor pulmonale resulting mainly from chronic affections of the lungs, there are subacute varieties resulting from secondary carcinoma in the lungs, and a now well-known acute

form resulting from pulmonary embolism. These varieties are indicated in the accompanying table.

TABLE

*Classification of Causes of Pulmonary Heart Disease  
(modified from Spain and Handler)*

1. ACUTE.—Massive Pulmonary Embolism.
2. SUBACUTE.—(a) Lymphatic miliary carcinomatosis.  
(b) Embolic carcinomatosis.
3. CHRONIC.—A. *Lung disease.*
  - (a) Emphysema Heart Disease
    - due to (i) Bronchitis.
    - (ii) Bronchiectasis.
    - (iii) Cystic Disease.
  - (b) Fibroid Lung
    - due to (i) Tuberculosis.
    - (ii) Scleroderma.
  - (c) Pneumoconiosis
    - due to (i) Silicosis.
    - (ii) Anthraco-silicosis.
- B. *Vascular Disorders of the Lungs.*
  - (a) Primary Pulmonary Hypertension.
  - (b) Recurrent Pulmonary Embolism.
- C. *Kyphoscoliosis.*

# I. EMPHYSEMA HEART

This is the commonest cause of pure right heart failure, and as it has been the subject of numerous investigations it will be described in some detail.

*Pathogenesis and Pathological Physiology.*—The simplest view of the nature of chronic emphysema heart disease is that it results from obstruction to the blood pressure through the lungs from the destruction to pulmonary capillaries. That the problem is not quite so simple may be argued from some quantitative considerations. Blumgart and Weiss (1928) have shown that the capacity of the lung vessels in health may be about three quarters of a litre of blood. The functioning part of the lung is essentially a capillary organ and the proportion of the lung blood in capillaries is very large, probably of the order of about 50 per cent. (de Burgh Daly). If we assume the average length of a pulmonary capillary to be one-tenth of a millimetre, then the cross-sectional area of the capillaries holding 375 c.c. of blood would be 37,500 sq.cm., or about 4 square yards. Now, the cross-sectional area of the pulmonary artery is about 8 sq.cm., a minute fraction of the cross-sectional area of the capillary bed. It follows that if the elimination of the pulmonary capillaries alone is to be held responsible for the creation of the high pressure in the pulmonary arterial tree, a quite enormous proportion of the capillaries would have to be destroyed. It seems highly probable that the obstruction of the lung circulation which develops in emphysema lies in the arterioles rather than in the capillaries.

These theoretical considerations have recently been put to the test by the development of techniques for the measurement of pulmonary arterial pressure in man. Cournand and his collaborators in New

York have been able to attach a sensitive manometer to the external end of a catheter, the tip of which lies in the right ventricle. The systolic pressure plateau recorded in this chamber is of course the same as the systolic pressure in the pulmonary artery. By this means they have found that the normal pulmonary arterial systolic pressure ranges from 18 to 30 mm. mercury. In patients with emphysema, before the development of venous congestion and heart failure, the pressure in the pulmonary artery is, in fact, often raised, thus confirming the long held opinions of clinicians and pathologists.

When we consider the degree of the pulmonary hypertension in relation to the severity of the causal pulmonary disease, however, it is clear that the exact mechanism by which the pulmonary pressure is raised still requires further study. Perhaps the best measure of the severity of anatomical damage to the lungs is the change in the percentage of residual air. In the normal subject the residual air constitutes 16-40 per cent. of the total lung volume (vital capacity plus residual air). In emphysema the residual air increases as the vital capacity declines, and, in severe cases, the residual air percentage may reach 70 per cent. or more of the total lung volume. If we take the figures obtained by Bloomfield and his co-workers (1946) and plot the residual air percentages against pulmonary systolic pressures, it is seen that there is no significant correlation (Fig.). There are some patients with emphysema who have a severe degree of damage judged by the residual air percentage, but in whom the pulmonary arterial pressure is not much raised or even within normal limits. On the other hand, high pulmonary pressures are found in cases with quite mild emphysema. Hickam and Cargill (1947) have demonstrated a feature of the pulmonary arterial pressure behaviour in emphysema which may be of much importance. When the normal human subject exercises mildly so as to double the resting output of the heart, the pulmonary arterial pressure does not rise. Similar exercise in emphysema with an increase in output of the heart will cause an additional large elevation of the already raised pulmonary pressure. It seems that the pulmonary vascular bed has become rigid and unable to adapt itself to carry at a normal pressure the increased pulmonary blood flow of exercise.

Obliteration of half the lung vascular bed by ligation of one pulmonary artery has long been known to produce no significant rise in pulmonary arterial pressure: this has been confirmed by Cournand and his colleagues in a study of patients submitted to pneumonectomy. It is thus clear that the cause of pulmonary hypertension in emphysema is unlikely to be the strictly anatomical capillary obliteration so often described. A further possible mechanism will be discussed later.

Besides the raised pulmonary arterial pressure there is another curious feature about emphysema heart disease which has been brought to light by heart-catheterisation studies; when the heart fails, the output is often high normal, or even above normal. The only exception

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to this seems to occur in the terminal phases when the blood pressure falls, and in these circumstances the cardiac output is low in proportion to the pressure. (Howarth, McMichael and Sharpey-Schafer, 1945; Richards, 1947.) The condition, therefore, falls into the group of *high output heart failure* previously defined (McMichael, 1946) which includes the heart failure of anæmia, Beri-beri (Dexter, 1947), and similar conditions determined by the presence of a "parasitic" circulation such as that seen in arteriovenous aneurysms and generalised

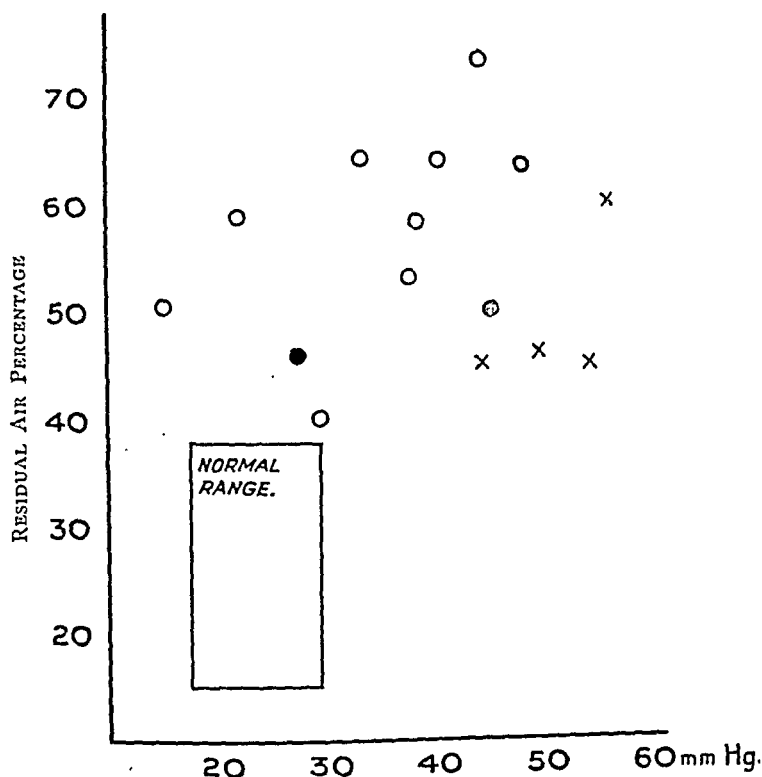


FIG.—The relationship of pulmonary systolic pressure and residual air percentage in emphysema, silicosis and pulmonary fibrosis (data from Bloomfield *et al.* 1946). In general the pulmonary systolic pressure is raised above the normal in this series. In emphysema there is a rough correlation, but cases are shown with residual air up to 60 per cent. where the pulmonary arterial pressure is within the normal range.

Paget's disease of bone (Edholm, Howarth and McMichael, 1946). The underlying mechanism of the raised output of the heart in emphysema and in anæmia may be similar, as in both conditions there is a deficiency of available oxygen in the arterial blood. The rise of venous pressure in these patients is best regarded as compensatory to maintain the cardiac output, and reduction of venous pressure by venesection may be harmful. The oxygen saturation of the arterial blood in patients with chronic emphysema and heart failure is nearly always below 80 per cent., and ranges widely below this value. We have seen patients with arterial oxygen saturation as low as 33 per cent.

*Clinical Manifestations.*—Most of the patients with emphysema heart disease are over forty. The breathless bronchitic whose dyspnoea persists between attacks has advanced to a stage at which emphysema is sufficiently pronounced to interfere with the normal oxygenation of his blood. Attacks of fainting and giddiness sometimes occur at this stage. Sooner or later evidence of right heart hypertrophy, and then failure with congestion and œdema, will complete the picture. The patient is dusky blue, his veins are congested, but in contrast to the patient with low output heart failure, whose extremities tend to be cold and blue, the hands, nose and ears are usually warm. The pulse is rapid (90-120) and is of good volume, as might be expected from the slightly raised cardiac output. A curious and interesting feature is the occasional presence of papilloedema and retinal hæmorrhages. Complicating exacerbations of bronchitis are often present and seem to be precipitating factors in determining failure. When there is accompanying asthma the patient is orthopnoic, but in some striking cases, without associated bronchial obstruction, he may be most comfortable in a completely recumbent position, even though venous engorgement is gross. Terminally hydrothorax and œdema may develop at the lung bases, a mechanical explanation of which is not easy to conceive. The cardiac output is usually falling at this stage and a general cardiac failure of a mal-oxygenated heart may be part of the terminal picture.

Apart from evidence of right hypertrophy, which may be difficult to detect clinically as the heart is often concealed by enlarged lungs, there is little to be made out on physical examination of the heart. Triple rhythm may sometimes be audible to the left of the sternum. A diastolic murmur of pulmonary insufficiency is rare. Radiologically, enlargement of the pulmonary artery is common, but it is only occasionally that right ventricular hypertrophy can be recognised with certainty in the X-ray picture. The electrocardiogram shows evidence of right ventricular preponderance, and this is often present before the other signs of right heart failure develop. Auricular fibrillation, which is an almost constant accompaniment of failure in mitral stenosis, is exceptional in emphysema heart, only occurring in about one case in ten.

*Other Special Investigations.*—The arterial blood may be grossly unsaturated with oxygen. Instead of the normal 95 per cent. saturation, values of 60-70 per cent. are common.

Examination of the oxygen unsaturation of a sample of arterial blood, which is a much simpler procedure than many clinicians imagine, may be a most useful diagnostic test. In most cases of left heart failure, even with œdema of the lungs, the oxygen saturation of the arterial blood seldom falls below 85 per cent. Unless the arterial oxygen saturation is below 80 per cent., it can be taken that emphysema is not sufficiently severe to play any part in the production of heart failure in that particular subject. Circulation time is often normal,

which is in contrast with the gross prolongations in low output heart failure. Polycythæmia is unusual, but it may sometimes be seen. It is worth while noting that arterial oxygen may fall much lower in severe congenital heart disease, while in emphysema, when the oxygen saturation is at its worst, there is often an exacerbation of acute bronchitis and infection may possibly interfere with bone-marrow activity.

*The course* is usually rapidly downhill. It is the exception for a patient to withstand more than two attacks of heart failure from emphysema. In this connection it is interesting to speculate on the possible influence of the coronary blood flow: systemic hypertension automatically increases the flow through the coronary arteries, but there is no such automatic regulation of the coronary supply in pulmonary hypertension. Müller (1937) has, in fact, shown that the right ventricle is much less capable of adapting to the increased work demanded by elevated resistance in the pulmonary arteries than the left ventricle is to a rise in systemic arterial pressure.

*Treatment.*—While digitalis and venesection increase the output of the heart in many cases of low output failure, these measures may have the opposite action, *i.e.* decrease in cardiac output, in many cases of chronic cor pulmonale (Howarth, McMichael and Sharpey-Schafer, 1947). This anomalous action of digitalis may be accounted for by the primary venous pressure reducing action of the drug which interferes with what may be a compensating mechanism maintaining cardiac output. In our experience venesection and digitalis have only raised the output of the heart in patients in whom the arterial pressure has fallen below 100 mm. mercury, and at this stage patients are often unlikely to make any satisfactory recovery. Digitalis and venesection, therefore, are unlikely to help and may even be dangerous. In most of these patients the attack of heart failure is precipitated by an exacerbation of bronchitis, and attention to this causal condition is more important than the use of standard cardiac remedies. An oxygen tent, in which the patient is kept continuously until his bronchitis has subsided, is the most valuable remedy. Bronchitis itself may be treated directly by aerosol penicillin inhalations.

#### ANOTHER TYPE OF CIRCULATORY FAILURE IN LUNG DISEASE

*Acute Circulatory Failure from Sudden Reduction of Negative Intra-thoracic Pressure.*—Patients with emphysema who develop superadded pneumothorax of the valvular variety, or who have a large bulla which may blow up in a similar manner, are likely to become acutely distressed with severe dyspnoea, gross air-hunger, and a pulse of poor volume and low pressure. In one such emphysematous patient who had a pneumothorax the intrathoracic pressure fluctuated round about zero, while the hydrostatic pressure in his right auricle remained extremely low. Filling of the heart, which normally takes place at an effective filling pressure of 7 cms. water (2 cms. hydrostatic

pressure plus 5 cms. negative intra-thoracic pressure), was grossly interfered with, and his cardiac output was 2.4 lit/min. (normal 5.3). In spite of the low output in this particular patient there was electrocardiographic and clinical evidence of right heart hypertrophy, showing that the raised pulmonary resistance is independent of the high cardiac output factor. This is a variety of acute circulatory failure which of course is easy to differentiate from chronic cor pulmonale with venous congestion.

## II. OTHER CLINICAL VARIETIES OF PULMONARY HEART DISEASE

1. ACUTE COR PULMONALE.—This condition, first clearly defined by McGinn and White (1935) results from blockage of the pulmonary arteries by emboli, the latter usually coming from the leg veins, following operations in the surgical wards, or in chronically ill and bedridden patients in the medical wards, especially those past middle life. It may complicate many ordinary forms of heart disease. The acute attack is often preceded by symptoms of smaller emboli in the periphery of the lungs causing pleural pain or hæmoptysis, but the actual development of right heart strain results from blockage of the large arteries at the root of the lungs without any of the manifestations of peripheral pulmonary embolism.

The patient becomes suddenly aware of a feeling of suffocation and apprehension, perhaps with a sensation of substernal oppression, but there is no actual pain. He develops air hunger, is pale and may sweat, while the pulse becomes small in volume and the blood pressure falls. The venous pressure is raised, as seen by Lewis's method of inspection of the neck veins, but in the collapsed stage it may require careful inspection to make this out. On examination of the heart there may be evidence of exaggerated pulsation of the right ventricle and at times a gallop rhythm may be heard in this region. The electrocardiogram is often diagnostic. The standard leads may simulate a posterior myocardial infarction of  $Q_3$   $T_3$  pattern, but precordial leads (C R or V leads) show inversion of T waves over the right ventricular region (Wood, 1941).

2. RECURRENT PULMONARY EMBOLISM.—Ljungdahl (1928) raised the question as to whether there was such a condition as chronic embolisation of the pulmonary arteries. He described two women, aged fifty-one and thirty-eight, who had suffered for years from a dry cough, slowly developing breathlessness and finally signs of heart failure. The right ventricle was enlarged and there was radiological enlargement of the pulmonary vascular shadow, but no other signs of valvular or other disease of the heart. At autopsy there was severe blocking of the pulmonary arteries with thrombi, with dilatation and hypertrophy of the right heart. The lungs appeared normal.

Three cases of this type have come under my notice in the past few years. Two, however, were somewhat complicated by other

factors (coronary disease in one, and empyema in the other), and I shall therefore only describe briefly the third case.

A woman, aged fifty-two, had been well until two years before admission to hospital. Following an attack of bronchitis she noted increasing shortness of breath on exertion, accompanied often by deep-seated pain under the right ribs (? hepatic congestion). This pain came on on effort and disappeared with rest. The dyspnoea steadily progressed and in the last two months she had difficulty in getting to her work as a typist. Four days before admission she came home from work feeling nauseated, with more severe pain, and dyspnoea worse than ever. She never had any hæmoptysis.

On examination she was restless and anxious with marked air-hunger. The lips were cyanotic, and the jugular veins were engorged 6 cms. above the sternal angle in the propped-up position. The apex beat was not easily palpable. A gallop rhythm was audible just internal to the mid-clavicular line and a systolic murmur was present over the tricuspid area. Blood pressure was 90/70. The legs showed extensive varicosities with thrombosis of the superficial veins and extensive scarring from old varicose ulcers. In addition a thrombosed cord could be felt in the middle of the left popliteal fossa. Sedimentation rate was 2 mm. in one hour and white cell count was 27,600.

A diagnosis of pulmonary embolism was made which was confirmed by characteristic electrocardiograms showing gross right preponderance and flat or inverted T waves in chest leads taken from the region of the right ventricle. Chest X-ray showed clear lung fields but the vascular shadows at the root of the lungs were considerably distended. The patient died suddenly two days after admission. Autopsy confirmed the diagnosis of pulmonary embolism. The heart weighed 480 gm. and there was gross hypertrophy of the right ventricle with no other demonstrable cause of heart failure, valves and coronary vessels being normal. Some of the emboli were very old and had become organised and recanalised. The source of emboli was traced in the popliteal and femoral veins.

In this case there had been some cause of obstruction of the pulmonary circulation acting for a considerable time to produce the degree of hypertrophy which was seen at post-mortem. No cause other than repeated pulmonary embolism could be found.

3. SUBACUTE COR PULMONALE FROM SECONDARY CARCINOMA IN THE LUNGS.—The term "subacute cor pulmonale" was first suggested by Brill and Robertson (1937) for this condition which develops in a few weeks or months. Greenspan (1934) reviewed the ways in which secondary carcinoma of the lungs might produce stresses on the right heart.

(1) Certain types of carcinoma may spread to the lungs as blood-borne emboli. Schmidt (1903) showed that tumour cells disintegrate in the lung vessels and surrounding thrombus becomes organised, with blockage of the lumen of the vessels.

(2) Greenspan records lymphangitis carcinomatosa of the lungs with accompanying obliterative endarteritis resulting from invasion of the lung vessels by carcinoma.

(3) Costedoat (1933) emphasised a suffocating form as distinct from an embolic form with a rapid pulse and dyspnœa and found no change in the lung vessels. This results from carcinomatous lymphangitis of the lungs.

A woman, aged sixty-seven, had carcinoma of the body of the pancreas. Miliary mottling was present in the lungs from January 1945, and the patient subsequently survived six months, during which time the mottling increased in size and density. Two weeks before her death the electrocardiogram showed definite signs of cor pulmonale, the arterial blood was 78 per cent. saturated with oxygen, and the cardiac output was 7 lit/min., a high figure for a small woman. Right auricular pressure was raised 2-3 cms. saline above the normal. This is an example of the suffocative form.

An example of the embolic form was seen recently in a woman who had had a miscarriage some four months before her death. She presented with heart failure, at first thought to be due to hyperthyroidism, but as time went on she developed clear signs of right heart stress. At post-mortem the lung vessels were extensively blocked by tumour emboli from a chorionepithelioma with secondary thrombosis.

4. PRIMARY PULMONARY HYPERTENSION.—There are now in the literature many instances of failure of the right ventricle with associated pulmonary vascular sclerosis usually described as cases of primary pulmonary hypertension. For a long time discussions on this subject were bedevilled by memories of "Ayerza's syndrome" in which a similar picture was said to be associated with polycythæmia and in the etiology of which syphilis was said to play a part. While this syndrome may occur it must be rare, and in South America competent observers are now inclined to stress its rarity. McCallum (1931) emphasises that the sclerosis affects the small arteries of the lungs (which were usually spared in mitral stenosis). Cases have been described in this country by de Nevasquez *et al.* (1940), East (1940) and Armstrong (1940).

A female, aged twenty-seven, developed dyspnœa over about a year. Investigation showed gross right ventricular enlargement with enlargement of the pulmonary artery. Pressure in the right auricle was 18 cms. saline above the sternal angle and the *mean* right ventricular pressure was 60 cms. above the same reference point. It is quite possible that her pulmonary systolic pressure was of the order of 80 mm. mercury. The illness was progressive and at post-mortem some twenty months after the onset of the illness, the small pulmonary arterioles were thickened and the right ventricle was grossly hypertrophied, but the picture was complicated by the presence of numerous pulmonary emboli. There was no bronchitis or emphysema.

Pulmonary embolism complicates very many instances of cardiac

failure, and where the primary cause lies in the pulmonary circulation the differential diagnosis between recurrent pulmonary embolism and primary pulmonary hypertension complicated by emboli may be a matter of considerable difficulty.

5. COR PULMONALE RESULTING FROM FIBROID CHANGES IN THE LUNGS.—(a) *Non-tuberculous Fibrosis*.—The fibroid changes which accompany such conditions as bronchiectasis are frequently accompanied by the development of right heart failure in a manner similar to that seen in chronic bronchitis.

(b) *Tuberculosis*.—Nemet and Rosenblatt (1937) have given an excellent review of the condition of the right heart in tuberculosis. In 71 patients who came to post-mortem in the tuberculosis service of the Montefiore Hospital they found right ventricular hypertrophy in 24 instances. Generally speaking, however, the heart was not increased in weight, and, in fact, was often reduced. The thickness of the right ventricle in moderate enlargement was 5·7 mm. and reached as high as 9 mm. Clinically the patients were cyanotic, the veins were often congested, and the usual symptoms of cardiac failure were present. Some of these patients had miliary tuberculosis which would possibly be a factor in raising pulmonary arterial pressure. They emphasise the difficulty of making a diagnosis in the absence of radiological cardiac enlargement.

(c) *Silicosis*.—Cor pulmonale is generally recognised as a terminal event in silicosis, but there are no recent detailed studies of its mode of development. Bloomfield and his group include a few pressure measurements in silicosis in their report (Fig. 1). My own experience is limited to a case which showed endarteritis of the pulmonary arteries at post-mortem.

(d) *Pulmonary Fibrosis in Scleroderma*.—The association of that form of scleroderma which shows itself predominantly in the fingers (sclerodactyly) with Raynaud's disease and visceral affections of the œsophagus, lungs and heart, is now well recognised (Weiss, Stead, Warren and Bailey, 1943). These authors show that the heart itself may be directly affected. The lungs, however, often show a diffuse fibrous change affecting the walls of the alveoli. Some authors (for example, Kraus 1924) have reported right heart hypertrophy as a consequence of the pulmonary change. I have seen one instance of this condition. An elderly female patient had suffered for some ten years from Raynaud's disease and also dysphagia. The hands were characteristic of sclerodactyly and there were typical œsophageal lesions. The lungs showed extensive diffuse fibrosis with a heavy accentuation at the right apex. For the last five years of her life she had a right ventricular preponderance in the electrocardiogram, and had frequent admission to hospital with breathlessness. She died outside hospital and there was no post-mortem.

6. COR PULMONALE IN KYPHOSCOLIOSIS.—This is a form of chronic cor pulmonale not widely recognised in this country. Excellent



reviews have appeared in America, especially those of Boas (1923) and Chapman, Dill and Graybiel (1939). In France and Germany the condition has been well recognised for a long time. Corvisart (1806) was familiar with the fact that the right heart was often dilated in kyphoscoliosis. Traube (1878) found at autopsy in a hunchback dilatation of the right ventricle, the patient having had typical symptoms of right heart failure before death. Boas describes the mechanism of these changes as follows:—

“The deformed thorax is smaller than normal in size and the diaphragm is usually high. Moreover, because of the fact that thoracic distortion is well established before bodily growth is completed, the chest lags behind the rest of the body in development. As a result of these factors the lung volume is steadily encroached upon with ensuing atelectasis of large pulmonary fields.”

By this means he thought the capillary bed of the lungs was reduced. Chapman and his colleagues found that the lung volume in these patients was in fact greatly reduced, but the mechanism by which the pressure in the pulmonary vascular bed was raised was uncertain. Our experience confirms the presence of changes in the right heart following on kyphoscoliosis. An example is seen in the following brief case record:

A patient, aged forty-four, with a gross dorsal kyphosis resulting from an old tuberculous spine was admitted to hospital in heart failure. He denied any significant bronchitis, and had never had a purulent sputum. Radiologically no fibroid changes were present in the lungs. He had gross venous congestion and right ventricular dominance was marked in the electrocardiogram. Cardiac output was 3.7 lit/min., but the blood pressure was 65/46 at the time, and he therefore showed reactions similar to those at the terminal stages of ordinary varieties of emphysema heart.

The patient died forty-eight hours after the observations were made. Autopsy showed gross right ventricular hypertrophy, but no significant bronchitis or pulmonary fibrosis.

#### DISCUSSION AND CONCLUSION

From the above survey it seems apparent that pulmonary heart failure develops largely as the result of hypertension in the pulmonary circulation. In a number of cases there is adequate evidence of pulmonary vascular obstruction—the *obstructive group*, but in others—the *anoxic group*—an anatomical cause of obstruction is absent. Some light may be shed on the problem by the recent work of Motley and his colleagues at the Bellevue Hospital. The inhalation of 10 per cent. oxygen in normal man immediately doubles the pulmonary arterial pressure without any accompanying change in cardiac output. This vaso-constrictive effect of low oxygen tension on the pulmonary arterioles has also been analysed by von Euler and Liljestrand, who have shown that it is not mediated by vaso-constrictor nerves, but is

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rather a local reaction of the pulmonary arterioles and pre-capillaries to oxygen lack. The latter authors suggest that this mechanism regulates the blood-flow through various parts of the lung according to the efficiency of aeration in each area. It is by this means that the circulation through atelectatic and pneumonic lobes may be closed off. Poor ventilation of the lungs may induce this vaso-constrictive reaction and this may be the key to the problem of many forms of pulmonary heart disease. The difficulty of moving a kyphoscoliotic thoracic cage with consequent limited ventilation may have the same action on the pulmonary arterial pressure as the poor ventilation of emphysematous lungs, or lungs in which the bronchioles and alveolar ducts are strangled by peri-bronchial lymphatic carcinoma.

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## HYDATID DISEASE \*

By D. M. DOUGLAS, *M.B.E.*, M.B., Ch.M., M.S. (Minn.), F.R.C.S.

THE clinical material upon which this lecture is based was in the main observed in the Royal Hospital, Baghdad, and, though the mode of propagation of the hydatid parasite is the same throughout the world, it may be of interest to describe the factors which are responsible for the endemic nature of the disease in Iraq.

The country can be divided into four economic zones. In the north are the highlands around Mosul, Kirkuk and Suleimaniya where the inhabitants, many of them Kurdish and Christian, engage in hill-farming and produce fruit, cereals and sheep. The second main source of employment here is oil production, and the oil wells, producing a high grade oil which is piped by a trans-desert pipe line straight to the Mediterranean, have been responsible for turning many hill tribesmen into expert oil engineers.

In the central zone, between the two rivers, lies the fertile Mesopotamian plain about which Herodotus in the fifth century B.C. wrote: " It will yield commonly two hundredfold or when production is greatest even three hundredfold. The blade of the wheat plant is often four fingers' breadth " (Government of Iraq, 1946). Although of the appearance of desert, the plain is in fact composed of rich alluvial soil washed down by the Tigris and Euphrates throughout the centuries. If provided with the necessary water by irrigation, it is capable of producing two good crops a year. The central zone is populated by the Fellahin who are for the most part Muslim Arabs. Under a feudal system of land tenure, they labour with great industry to produce their crops of wheat, barley, maize and lentils. Their implements are primitive in the extreme, and the picture of an Arab farmer tilling his fields with a wooden plough drawn by two donkeys is one which has not changed materially since his forefathers watched Xenophon and the Ten Thousand march towards the Black Sea. Sheep are raised in large numbers in this zone and round the mud-built farm communities dogs, sheep and children live together in close propinquity and with a pleasant lack of hygienic restrictions.

The third zone is the western desert which stretches for 400 miles to Damascus. Arid except for an occasional oasis, it is the home of the Beduin Arabs who, though owning no land, yet recognise no frontier and move at will from Iraq to Syria, Transjordan and Saudi Arabia. The camel is the centre of their economic life. Ghee from camel milk is used for cooking the rice, wheat and dates, which they

\* A Honyman Gillespie Lecture delivered in the Royal Infirmary, Edinburgh, on 22nd May 1947.

obtain by the sale of camel hair. They eat meat only on such special occasions as tribal feasts or celebrations. Gazelle hunted with hawk and saluki supplement the diet from time to time.

Finally, the marsh lands of the south are inhabited by a semi-aquatic people who grow rice in the flooded fields and tend their water-buffaloes from boats. Bilharziasis and ankylostomiasis are endemic here and cause a severe form of anæmia which gives to the Arab skin a very characteristic greyish pallor. In the south as in the central zone dates are cultivated in great numbers, and in fact three-quarters of the date palms in the world are grown in Iraq (Government of Iraq, 1946).

It is in the central zone that hydatid disease is endemic. Here the necessary links in the hydatid chain are complete; the parasite can pass from dog to sheep or man with facility and finally return to dog by the ingestion of sheep viscera.

#### BIOLOGY OF THE HYDATID PARASITE (Dew, 1928)

The parasite exists in two forms, as a tapeworm and as a cyst. The tapeworm, *Tenia echinococcus*, is about 5 mm. long and possesses a head and three segments. The head is equipped with a retractable rostellum, two rows of hooklets and four sucking pads with which it is enabled to adhere to the mucosa of the small intestine. The terminal segment, known as the proglottis, contains the organs of generation, and when filled with ova, is shed into the fæcal stream, thus transporting the ova to the exterior.

The ova, known as the hexacanth because they possess six hooklets, are enclosed in chitinous envelopes which are resistant to physical agencies but are readily dissolved by the gastric juice of the sheep or of man after ingestion. The ova are thus liberated and, adhering to the walls of the stomach and small bowel by their hooklets, they burrow into a portal radicle and are carried to the liver. There the majority are held up in the hepatic capillaries but a few pass through to the inferior vena cava and reach the lungs. Still fewer ova pass through the pulmonary capillaries and reach the systemic circulation.

**DEVELOPMENT OF THE CYSTIC FORM.**—The hexacanth ovum, being caught up in a capillary, thereupon develops into an adult hydatid cyst by a gradual process which takes perhaps many years. It has been said that a mature cyst is almost as old as its host.

First a cellular reaction occurs around the parasite which gradually becomes differentiated into three zones—a peripheral zone consisting of fibroblasts arranged in a concentric manner, an intermediate zone of radially arranged endothelial cells and an inner zone of round cells and eosinophils. Meanwhile the parasite itself becomes vacuolated. The vesicle becomes lined with a single layer of germinal nucleated epithelium and underlying it the round cell and endothelial layer

becomes replaced by layers of hyalin material—the laminated layer. The peripheral zone becomes firmly interfused with the tissues of the host and is known as the adventitia or ectocyst.

DEVELOPMENT OF BROOD CAPSULES AND SCOLICES.—A further stage of development is necessary before the cyst becomes fertile—the development of brood capsules containing scolices. At several points on the nucleated germinal layer, cell multiplication takes place to form nodes. The nodes become vacuolated, pedunculated and project into the lumen of the cyst. These are the brood capsules. In due course nodal thickening occurs in the lining of the brood capsule and these areas of thickening develop into scolices which project into the brood capsule.

The scolex possesses a retractile head with suckers and hooklets and an elongated body containing calcareous particles whose function is unknown. When ingested by the dog, it adheres to the mucosa of the small bowel and becomes the adult *Tænia echinococcus*. The adult simple hydatid cyst is therefore far from simple in its composition, possessing three layers—the adventitial, laminated and germinal layers and two additional structures, the brood capsules and the scolices. Hydatid fluid, which fills the cyst and protects and nourishes the brood capsules, is clear and colourless, of a specific gravity of 1010 and containing a trace of albumin and sugar. Its osmotic tension is similar to that of plasma.

DEVELOPMENT OF DAUGHTER CYSTS.—The majority of hydatid cysts in adult patients are multilocular and there has been much dispute as to the nature of this further development.

There appears to be little doubt that the development is protective in function. Following upon fragmentation of the germinal layer, the separate portions proceed to lay down a laminated layer around themselves and hence to develop into complete new cysts within the old cyst. Thus the viability of the parasite is assured. The agency which causes fragmentation of the germinal layer may be direct trauma, such as that caused by a needle puncture or a blow on the parietes, or the growth of the cyst against a relatively resistant structure such as a bile duct.

### THE HYDATID CYCLE IN IRAQ

Briefly to recapitulate the hydatid cycle in Iraq, a dog eats sheep viscera containing hydatid cysts (Fig. 1). By means of their hooklets, the ingested scolices adhere to the small intestine of the dog. There they develop into adult *tæniæ*. When the terminal segment or proglottis of the *tænia* becomes mature and filled with ova, it is shed and passes into the faecal stream. At this point the ova may be ingested by sheep in contaminated grass or by man through handling the coat of the sheep dog. In either case the ova pass to the stomach where the chitinous envelope is dissolved by the gastric juice and the

hexacanth liberated. After burrowing its way through the mucosa, it is carried by a portal radicle to the liver where the adult cyst develops.

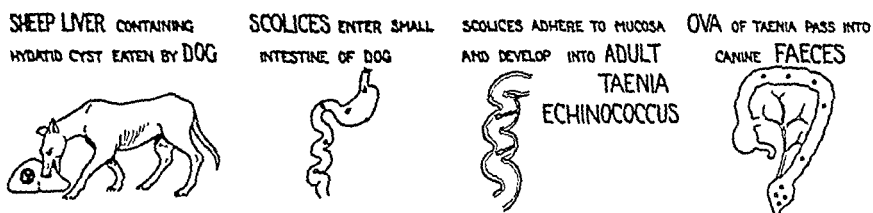
### GENERAL FEATURES OF HYDATID DISEASE IN MAN

A hydatid cyst exercises all its effects either as a space-occupying lesion or by means of the complications to which it is liable.

**PRESSURE EFFECTS.**—As a space-occupying lesion it may attain great size in the liver or lung without causing symptoms, but when

## LIFE CYCLE OF HYDATID PARASITE IN IRAQ

### A. DEFINITE HOST—DOG



### B. INTERMEDIATE HOST—SHEEP AND MAN

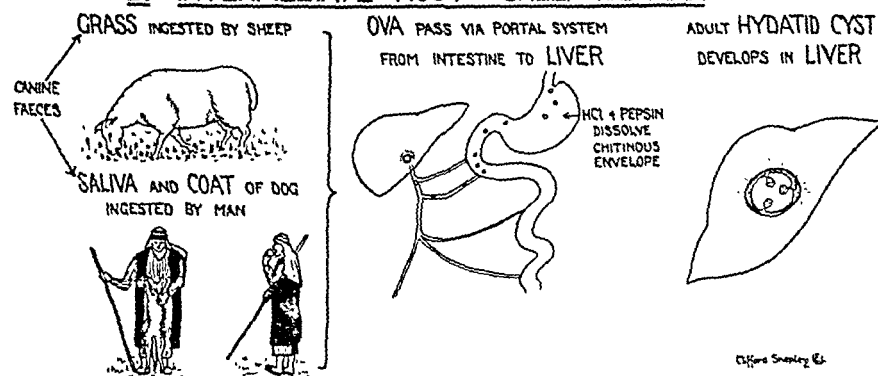


FIG. 1.—Life cycle of hydatid parasite in Iraq.

its growth is confined by bone, as in the central nervous system, symptoms are early and marked.

A girl of nine years was admitted to Dundee Royal Infirmary in July 1934, under the care of the late Professor John Anderson, complaining of pain and progressive weakness in the legs for nine months. Neurological examination revealed a picture characteristic of a lesion of the cauda equina. There was wasting and weakness in both calf muscles and loss of the ankle jerks. An area of impaired sensation was present around the anus. There was some difficulty in completely emptying the bladder. Myelography showed a prolonged hold up of the medium at the level of the second lumbar vertebra.

On 26th June 1934, laminectomy was performed by the late Professor John Anderson and a greyish cystic swelling was found lying in the extradural space. It was easily lifted out but in so doing ruptured, allowing clear fluid to escape.



Pathological report was "Hydatid Cyst." The patient made a rapid recovery and when seen six months later was free from symptoms. X-ray showed that some lipiodol was present but that it had passed down into the lower end of the theca.

Two other cases of intrathecal hydatids were seen at the Royal Hospital, Baghdad, both of a peculiar "dumb-bell" shape communicating through the intervertebral foramen to another compartment

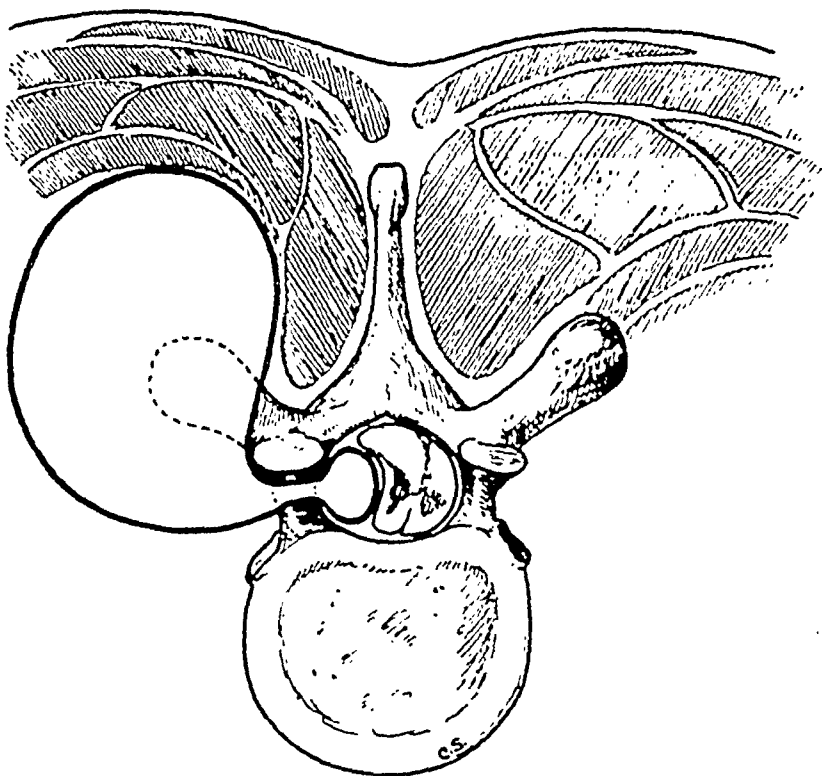


FIG. 2.—Diagrammatic representation of intrathecal hydatid cyst at level of tenth thoracic vertebra with protrusion through intervertebral foramen into paravertebral muscles.

lying in the paravertebral muscles (Fig. 2). In both there was erosion of the adjacent pedicles.

A young Arab of some thirty years was admitted to the Royal Hospital, Baghdad. He was referred for surgical treatment by Dr Jack Aboody. He gave a history of pain in the back radiating round the abdomen and progressive stiffness and weakness in the legs. There was difficulty in emptying the bladder.

*Neurological examination* showed loss of the abdominal reflexes, exaggeration of all deep reflexes in both lower limbs, and extensor plantar responses. Motor power was still present in both legs but insufficient to allow the patient to walk. The loss of motor power was greatest on the right side. A zone of hyperæsthesia was present around the trunk at the level of the eighth thoracic segment.

A fluctuant swelling was present in the paravertebral muscles on the right side at the level of the tenth dorsal vertebra, and *myelography* with lipiodol showed a block at that level.

In spite of the absence of radiological evidence of disease of the vertebræ, a diagnosis of an intrathecal cold abscess with a secondary posterior paravertebral abscess was made and exploration advised.

At laminectomy an intrathecal hydatid cyst with an extension through the intervertebral foramen into the paravertebral muscles was found and easily removed, not however without rupture. The patient made a good immediate recovery and was able to walk when discharged. Recurrence is, however, very likely.

The third case was a middle-aged Arab with a very extensive hydatid cyst in the suboccipital region communicating with an intrathecal cyst through the foramen between the second and third cervical vertebræ. An incomplete

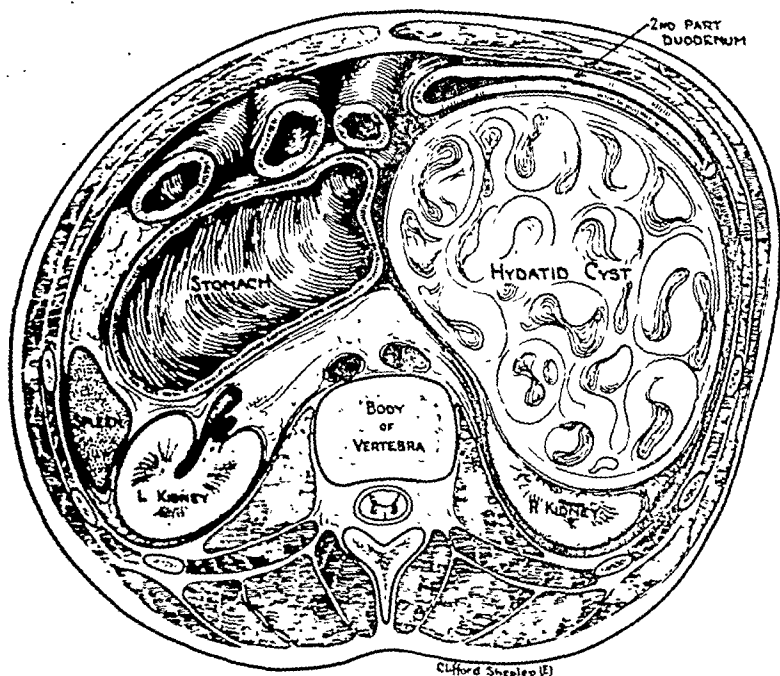


FIG. 3.—Diagrammatic representation of hydatid cyst of right kidney producing duodenal obstruction and vomiting.

quadriplegia. was present with spastic contractures of his lower limbs. Laminectomy was carried out but it was not possible completely to remove the extrathecal extension and no improvement followed the operation.

An unusual type of pressure effect was seen in the following case of renal hydatid.

A middle-aged Arab woman was admitted to the Royal Hospital, Baghdad, complaining of vomiting, loss of weight and a swelling in her right side.

On examination the swelling was obviously a greatly enlarged right kidney and a pyelogram showed compression and deformation of the right renal pelvis. The Casoni reaction was positive.

The kidney was exposed through an anterior approach by a transverse incision with a short vertical limb at the inner end. The cause of the vomiting was soon apparent (Fig. 3). The descending part of the duodenum was

stretched over the front of the tumour as a wide band and an almost complete duodenal stenosis was present. Great care was taken in dissecting the duodenum off the tumour, but in spite of this the blood supply to the wall of that structure must have been jeopardised; a duodenal fistula developed at the end of a week from which the patient died.

### EFFECTS OF COMPLICATIONS

The two chief complications to which hydatid cysts are prone are (a) rupture and (b) infection.

(a) *Rupture*.—Rupture of a hydatid may lead to further dissemination which is common, or to spontaneous cure which is less common. Spontaneous cure may occur in hepatic cases after intrabiliary or intra-intestinal rupture.

An Iraqi soldier of thirty years was admitted to the Royal Hospital with a recurrent swelling of the upper abdomen. One year before he had been operated on in a military hospital for a hydatid cyst of the liver.

The liver was found to be very much enlarged and lobulated, tense but not tender. An incisional hernia through a Kocher's incision was present. Casoni reaction was positive. At re-operation a large hydatid cyst of the right lobe of the liver was present with the hepatic flexure and right half of the transverse colon firmly adherent to it. A smaller hydatid of the left lobe was present. In view of the danger of injury to the colon, the larger cyst was not interfered with. The cyst in the left lobe was marsupialised and the laminated and germinal layers removed. He made a good recovery from this operation. Six months later he returned to hospital and reported that after a severe attack of abdominal pain he had passed large quantities of membranous material by the rectum. His abdominal swelling had disappeared after this. On palpation no sign of the previous swelling could be felt.

**INTRAPERITONEAL RUPTURE.**—Rupture of a hepatic cyst into the free peritoneal cavity is an unhappy event which leads inevitably to dissemination of the disease. The symptoms resemble closely those of rupture of a hollow viscus and the case is usually diagnosed as such. On laparotomy daughter cysts and hydatid material are found in the free peritoneal cavity. Collapse is often extreme and urticaria may develop within a few hours or days. With multiple peritoneal hydatid cysts as the sequel, the patient's chances of a cure are remote.

**INTRABILIARY RUPTURE.**—Intrabiliary rupture results in biliary colic and jaundice—the symptoms of a stone in the common duct. The rupture usually occurs by pressure on a main branch of a hepatic duct, but occasionally occurs into the gall-bladder. The distinguishing feature of the condition is that cyst remnants are eventually passed per rectum.

Biliary colic and jaundice in a hydatid zone must lead to a search of the stools for hydatid material.

Spontaneous cure by rupture is most common in deep para-bronchial

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cysts of the lung. For this reason surgical operation is not as a rule advised in these cysts. The sub-pleural cysts, on the other hand, being remote from the main bronchi, do not often undergo spontaneous cure and surgery is usually undertaken.

The following is a case of spontaneous cure of a pulmonary hydatid cyst.

A young Baghdadi complained of a persistent non-productive cough. He was X-rayed and found to have a hydatid cyst of the right lung measuring 7 cm. by 7 cm. There was a small calcified cyst in the liver. It was likely that the pulmonary hydatid was the result of intrathoracic rupture of the now calcified hepatic cyst. He was advised to consult a famous European chest surgeon and travelled to a European capital for this purpose. While waiting for an appointment, he had an attack of coughing and brought up large quantities of hydatid material. When seen the following day, surgical operation was not advised and he returned to Baghdad. He then developed purulent expectoration and ran a temperature; the cyst had evidently become infected from the bronchial tree. Postural drainage in hospital resulted in cessation of the purulent sputum and disappearance of the pyrexia. Six years later he was X-rayed and no sign of the pulmonary cyst was present though the calcified hepatic cyst was unchanged. His health had remained excellent.

(b) *Infection*.—The mechanism whereby organisms gain access to a hydatid cyst is unknown, but it is likely that in the case of hepatic hydatids it is by bile which leaks into the cyst after a limited rupture. In the case of hydatid cysts of the lung, the entry of small amounts of bronchial secretion from an eroded bronchus may presumably have the same effect.

Once the cyst becomes infected, the inflammatory process proceeds to suppuration and the parasite usually dies. But the signs of a closed abscess become evident. Pain and tenderness are present, pyrexia is persistent and, if unrelieved, cachexia and wasting develop.

The risk of rupture is ever present. Intraperitoneal rupture leading to peritonitis or intrathoracic rupture leading to empyema is not infrequently the terminal event in the long history of the illness.

True suppuration must be distinguished from the aseptic degeneration which is sometimes seen. The yellowish debris which fills the cyst is indistinguishable macroscopically from pus. Microscopically, however, it is seen to be completely amorphous material and is sterile on culture.

It may be noted in passing that successful drainage of an infected cyst usually results in a cure because of previous death of the parasite.

*ANAPHYLAXIS*.—Hydatid anaphylactic shock has received much notice in text-books but in practice it is of little importance. Two phases appear to develop. Immediately following rupture of a cyst a condition of circulatory collapse may develop, often referred to as "shock." The blood pressure is low and the pulse of poor volume

or imperceptible. The second phase develops after several days when urticaria and generalised pruritus may develop.

Both phases are passing episodes in the more serious condition of rupture of the cyst.

### SPECIAL DIAGNOSTIC METHODS IN HYDATID DISEASE

1. SPECIFIC REACTIONS—(a) *The Casoni Reaction*.—Discovered in Tripoli in 1911, the Casoni reaction is the best of the special diagnostic



FIG. 4.—X-ray appearance of diaphragm and chest of a patient with primary hydatid disease of the liver and secondary cysts in the lungs. The elevation of the right cupola of the diaphragm is well seen. Note the "peri-vesicular pneumonia" at the upper margin of the large pulmonary cyst.

methods. The principle of the test is that the patient becomes sensitised to the hydatid fluid of his own cyst after minimal leakage and consequently the intradermal injection of a minute amount of sterile hydatid fluid produces a wheal and flare. A positive reaction is bi-phasic. In ten to twenty minutes after the injection a white wheal 3-5 cm. in size develops surrounded by a zone of erythema. The delayed reaction shows in eight to twelve hours and consists of a large area of erythema 5-6 in. in diameter and lasting twenty-four to seventy-two hours.

The Casoni reaction is positive in from 70 to 90 per cent. of cases. Where it is negative in a case of proved hydatid disease, it is believed

that the patient has been "desensitised" by massive leaks of fluid from his own cyst. False positives are obtained when the antigen from the sheep hydatid is impure and in cases of urticaria, asthma and dermatographism.

(b) *The Complement Fixation Reaction*.—This reaction, associated with the name of Weinberg, is analogous to the Wassermann reaction in syphilis. Antibody circulating in the patient's blood combines with antigen to fix complement and prevent hæmolysis in a sensitised sheep's cells system.

The complement fixation reaction is of special value when the Casoni reaction is negative through desensitisation, and it is always worth while to do both.

2. **RADIOGRAPHY**.—Radiographic examination is of the greatest value in hydatid disease. In hepatic cysts, elevation of the right cupola of the diaphragm is frequently seen (Fig. 4). In the lungs, the rounded shadow of a hydatid is not likely to be mistaken for any other lesion, particularly if a perivesicular rim of air is present (Davidson, 1944). In bone the multilocular appearance may stimulate an osteoclastoma or an area of localised osteitis fibrosa cystica. A rounded filling defect may be seen in the pyelogram in cases of renal hydatid.

3. **WHITE CELL COUNT**.—Eosinophilia is of value only where helminthiasis of other types can be excluded. This is seldom the case in Iraq where infestations with ascaris and ankylostoma are common. In Great Britain the presence of 5-15 per cent. of eosinophils in a differential count, where a hydatid cyst is suspected, is valuable circumstantial evidence.

### GENERAL DIAGNOSTIC METHODS

1. **GEOGRAPHICAL SITUATION**.—Hydatid disease should be suspected when a rounded tumour in any position is seen in a hydatid zone. A subcutaneous tumour which in Britain would be dismissed as a lipoma may well turn out to be a hydatid cyst in Iraq.

2. **ASPIRATION**.—This is mentioned only to be condemned. Aspiration may lead to leakage from the cyst and dissemination of the disease.

3. **THE HYDATID THRILL**.—Fluctuation can be obtained in hydatid cysts as in other cysts, but is usually not marked because of the great tension within the cyst. Where daughter cysts are present, a thrill, said to be proper to hydatid disease, is sometimes obtained but it is of unusual occurrence and of doubtful value in diagnosis.

### ANATOMICAL DISTRIBUTION OF HYDATID CYSTS IN MAN

Between 1942 and 1946, 140 cases of hydatid disease were treated surgically in the Royal Hospital, Baghdad (Table). As is usual, the great majority of cysts occurred in the liver and lungs. An unusual



number of renal hydatids were seen and the two intrathecal hydatids were quite exceptional. It is to be noted that these figures are not a true reflection of the distribution of hydatid disease in Iraq, since they comprise only those cases that were treated surgically. A true distribution table would certainly show several cases of hydatid disease of bone and brain.

TABLE

*Anatomical Distribution of 140 Hydatid Cysts in Patients admitted to Royal Hospital, Baghdad, 1942-46*

Site.	Number.	Per cent.
Liver . . . . .	86	61.5
Lung . . . . .	21	15.0
Kidney . . . . .	10	7.2
Peritoneum . . . . .	8	5.7
Muscle . . . . .	7	5.0
Spleen . . . . .	2	1.4
Theca . . . . .	2	1.4
Ovary . . . . .	1	0.7
Orbit . . . . .	1	0.7
Subcutaneous . . . . .	2	1.4
Total . . . . .	140	100.0

Nevertheless, the lesson is clear, 107 of the 140 cases occurred in liver and lungs, the primary and secondary capillary filters.

#### CLINICAL FEATURES OF HEPATIC HYDATID CYSTS

The existence of a simple hydatid cyst of the liver is compatible with, and is usually accompanied by, normal health in the host. There does not appear to be any toxin elaborated by the parasite nor does it rob the host of an appreciable part of his nutriment. Because of the fact that the liver can enlarge upwards and downwards with ease, pressure effects are not often seen. The uncomplicated hepatic hydatid and the host then achieve a state of peaceful symbiosis.

The diagnosis is usually made accidentally by the palpating hand of a patient or his doctor, as in the following case.

An Italian prisoner of war of thirty-five years was admitted to a military hospital with the history that his medical officer had discovered a mass in the epigastrium on routine skin inspection.

On examination a rounded swelling continuous with the liver was present in the epigastrium, and X-ray showed an extra-gastric mass displacing the pylorus downwards. At laparotomy a hydatid cyst of the antero-inferior border of the right lobe of the liver was discovered.

It is with the onset of complications that frank clinical features appear. These have already been referred to in the section on General Features.

## CLINICAL FEATURES OF PULMONARY HYDATIDS

As in the case of hepatic cysts, pulmonary hydatids may attain a considerable size without symptoms; when symptoms do appear they indicate involvement of a bronchus. An irritative, non-productive cough is the commonest symptom and not infrequently hæmoptysis appears later. Pain is not common and usually indicates a distal area of collapse with pneumonitis. The pain is of a pleuritic type, being made worse by deep respiration and coughing; dyspnœa is rarely seen.

Thus the symptoms of an uncomplicated pulmonary hydatid are not specific and the diagnosis rests on X-rays and special investigations. Pulmonary tuberculosis and bronchogenic carcinoma are the chief conditions which may give rise to difficulty in differential diagnosis.

The specific symptom of pulmonary hydatid disease is the coughing up of "grape-skins"—portions of the endocyst—which follows intrabronchial rupture.

## TREATMENT OF HYDATID DISEASE

No form of systemic treatment has been discovered which will alter the course of hydatid disease and this is not surprising when one considers the impermeable character of the laminated layer.

Prophylaxis is outwith the scope of this lecture, but it is obvious that if dogs were denied access to sheep viscera, or if children were denied access to dogs, the disease in man would rapidly die out. The aim of surgical treatment is quite simple—it is the elimination of all germinal tissue from the cyst without spillage. The accomplishment of this aim is far from easy. Total excision of the intact cyst is obviously the most efficient treatment, but this is possible only when the cyst is pedunculated, when it is present in a non-essential organ such as spleen or ovary, or when it is lying in a position where a block removal of tissue is possible.

**TREATMENT OF HEPATIC CYSTS.**—The silent nature of an uncomplicated hepatic hydatid and the perfect health of the host often made the writer wonder as to whether surgical treatment was indicated at this stage. But the risk of rupture and infection is so considerable and the management of a simple cyst so much easier than the management of its complications that one was driven to the conclusion that operation should be advised in all cases of hepatic hydatids.

The incision should be placed directly over the swelling, an easy matter in the case of antero-inferior cysts but extremely difficult in the case of superior and posterior cysts. The transpleural approach is associated with a great risk of infection of the pleura and a heavy mortality.

The cyst being exposed, it is customary carefully to pack off the wound with gauze soaked in 1 per cent. formalin in saline. A fine needle is then inserted into the cyst and 50 c.c. of fluid removed, 20 c.c. of 40 per cent. formalin being injected down the same needle. After an interval of ten minutes, the adventitia is incised and the

whitish laminated layer immediately prolapses. An attempt, invariably unavailing, is made to remove the laminated layer *en masse*; daughter cysts are almost always present, and a laborious piecemeal removal is necessary. The cavity is temporarily packed with gauze wrung out of 1 per cent. formal-saline and the gauze rotated, thus enmeshing any fragments which have been left behind. Finally the cavity is swabbed out with gauze soaked in alcohol, and the adventitia is closed without drainage. The cavity fills with serum and blood clot. The packs having been removed, the abdominal wall is then closed.

The technique is varied if the cyst is found to be infected when the preliminary aspiration is performed. Instead of opening the free cyst, the adventitia is stitched carefully to the parietal peritoneum in a complete circle and the cyst opened through the centre of the circle. After evacuation of the contents, a drainage tube is inserted. A sinus which discharges pus results, and continues to discharge, in the writer's experience, for many months.

The problem of evacuation of "dome" cysts is still unsolved. A certain number may be approached extraperitoneally, by Ochsner's approach after removal of the twelfth rib, but sometimes a transpleural approach after removal of a segment of the ninth or tenth rib is necessary. The operation is done in two stages, an iodine pack being placed against the parietal pleura at the first stage, a portion of one or two ribs over the cyst having been removed. At the second stage, fourteen days later, the diaphragm is incised and the cyst opened as before and the contents removed. As a rule primary closure of the adventitia is indicated unless the cyst is infected. The diaphragm is resutured and the wound closed. If the cyst is found to be infected, it is necessary to leave a drain in the cavity and the risk of pyo-thorax is thereby increased.

**TREATMENT OF INTRAPERITONEAL RUPTURE.**—The condition of intraperitoneal rupture of a hepatic cyst is rarely diagnosed before operation. As a rule the abdomen is opened to locate and suture a perforation of a gastric or duodenal ulcer, and the peritoneal cavity is found to contain daughter cysts and hydatid fluid. The management of this catastrophe is very difficult since it is impossible completely to remove all remnants of germinal tissue from the peritoneal cavity. As much material as possible should be removed by suction and swabbing, and the primary cyst carefully evacuated and closed. Recurrence in the peritoneal cavity is almost inevitable.

**MANAGEMENT OF PULMONARY CYSTS.**—There is a growing body of opinion that in pulmonary hydatids surgery should be reserved for subpleural cysts (Barnett, 1945). The deep cysts should be treated conservatively because of the considerable chance of spontaneous cure after intrabronchial rupture and evacuation by coughing.

Of the many methods that have been advocated for the treatment of subpleural cysts, two are worthy of mention.

The first is the two-stage evacuation similar to that described for

the "dome" cysts of the liver. This is the standard method and since daughter cyst formation is rare in the thorax, a satisfactory evacuation of the cyst can be obtained. The adventitia may then be closed by suture. If the cyst should prove to be infected, it must of course be drained and the risk of empyema is then considerable.

The second method is that of resection of the lobe containing the cyst (Barnett, 1945; D'Abreu, 1937; D'Abreu and Rogers, 1944). On rational grounds this is the ideal method because the risk of spillage is theoretically eliminated. It must be restricted to solitary cysts, however, and there is some danger of rupturing the cyst during dissection of the lobe, with consequent dissemination in the pleural cavity.

After spontaneous evacuation by intrabronchial rupture, infection of the cavity is not uncommon and the symptoms of a lung abscess may appear—expectoration of foul-smelling pus, intermittent pyrexia, and toxæmia. The condition should be treated *secundem artem* by postural drainage and inhalations, and the majority of patients respond satisfactorily to this regime. A small proportion continue to have symptoms and require transpleural drainage by a two-stage method.

### SUMMARY

1. Hydatid disease is endemic among the farming community of the central plain of Iraq.

2. The propinquity of sheep, dogs and children without hygienic restrictions provides the necessary cycle for the propagation of the parasite.

3. The uncomplicated hydatid cyst causes little trouble to its host, being a silent and unobtrusive guest, but the onset of complications makes it approximate cancer in its ultimate morbidity and mortality.

4. The aim of treatment is the elimination of the germinal layer of the cyst without spillage. In the present state of our knowledge this can be accomplished only by surgical means. At its worst, surgery may hasten the end by dissemination of daughter cysts; at best recurrence after surgery is by no means rare.

### ACKNOWLEDGMENTS

It is a pleasure to express my indebtedness to Dr Abdul Rahman Chorbachi, Sub-Dean of the Royal Hospital, Baghdad, to Dr Ghanim Akrawi and Dr Kadhim Shubbar for help in the preparation of this lecture, and to Dr H. J. C. Gibson, Medical Superintendent, Royal Infirmary, Dundee, for the notes of a case seen in the Royal Infirmary, Dundee.

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## STUDIES IN AMNESIA \*

By W. RITCHIE RUSSELL, M.D. (Edin.), F.R.C.P.

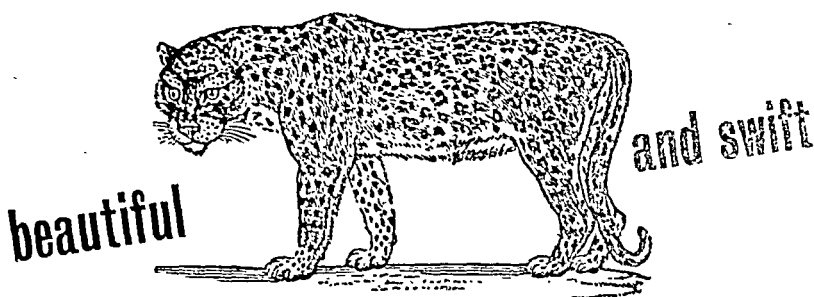
THE effects of head injury on the mechanism of remembering are of both academic interest and of practical importance. The classification of cases of cerebral trauma according to the duration of post-traumatic amnesia (Russell, 1932) is now widely practised and has been found of value in assessing the likely extent of disability after head injuries of varying degree (Symonds and Russell, 1943).

The clinical pictures observed during recovery from traumatic unconsciousness are of great interest to those who study the mechanisms of the brain, and some knowledge of the various phenomena observed must add interest to the surgeon or physician who is concerned with the care of these cases.

The factors which determine whether an observed event or a sensation experienced is remembered must be various. For example, it is clearly important in this connection whether the event is unusual, whether it stimulates the emotions, or whether a special mental effort is being made to remember what is seen or heard. If we see a street accident, the occipital cortex deploys the visual picture to neuronal systems in such a way that within a very short space of time the emotional hypothalamic mechanism is stimulated and the well-known bodily sensations associated with fear result. There will also be a direct relay to the motor system leading to a sudden start or a scream. It should be noted in passing that the brain recognises with remarkable speed that the incident demands relay to the hypothalamus and motor system. There is little time for reason to play a part here, and one can only assume that the unexpected, unusual or surprising event short-circuits other mental mechanisms to achieve the quickest possible defence reaction. In the young child most events are novel and the quick childish emotional response is familiar to us all, but as our years advance it becomes increasingly difficult for events to stimulate the emotions. We devise some means of dealing with them, without disturbing the hypothalamus.

Once the seeing of this street accident has stimulated the hypothalamus a highly complex system comes in to play, for, through the thalamus, the hypothalamus projects on all parts of the pre-frontal lobes (Le Gros Clark, 1948), and probably our behaviour in the emergency is to a large extent directed by the frontal lobes. This fronto-thalamo-hypothalamic mechanism is, of course, much more than an inhibiting mechanism which prevents us from, say, running away.

\* A Honyman Gillespie Lecture delivered in the Royal Infirmary, 30th October 1947.



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It also enables us to elaborate and exploit our emotional drive to produce perhaps in some people a superhuman response to deal with the emergency (Russell, 1948). The next question that arises is how is the image of the accident preserved for future recall. There is no reason to doubt the view expressed by Ferrier (1878) and Bain last century that the organic basis of recollection is simply the re-excitability of the original experience. That is to say when we recall the street accident we make use of the same neuronal circuits which were opened up at the time of the incident.

These comments, though partly hypothetical, give a convenient basis on which to attempt to interpret the phenomena of traumatic amnesia.

The stages of recovering consciousness after concussion indicate that there are many levels of mental activity, and that the most complex recover last. It is quite evident, for example, that behaviour may become almost normal while the patient is still unable to record events in such a way that they can be later recalled. Some of you will remember a surgeon in this hospital who, after a head injury, instructed a junior colleague where to trephine his skull. History does not relate whether his colleague realised that his chief was still confused, but the operation was duly carried out. The whole conversation, however, fell within the period of traumatic amnesia and the surgeon was never able to recall giving these instructions to his colleague. We are all familiar with cases of this kind, and they clearly indicate that the ability to remember current events is very high in the order of mental processes. This is confirmed by the specific loss of recent memory in old age and in a variety of toxic conditions. Outwardly normal behaviour with subsequent amnesia for current events is, however, associated with some impairment of the mental faculties in addition to loss of current memory, and the patient's response to a situation requiring some thought clearly brings out the defects in such a case. Indeed he is often disorientated in time and place, and may, for example, after being concussed while playing football, play towards the wrong goal. By the time the brain has recovered its full power of understanding, current events are well remembered and the period of post-traumatic amnesia has ended.

In cases of moderate concussion special events may subsequently break out of the amnesic period. For example, the visit of a relative or an operation may constitute an island of memory. Another example is that of the pilot of an aircraft who, after a crash, remembered turning off the petrol, but nothing more for many hours. Further, if a patient after concussion is questioned during the period of confusion he is sometimes able to tell more about the accident than he can remember after recovery, though his story may be elaborated by confabulation and even false accusations.

A specially interesting phenomenon is the occurrence of a recurring hallucination relative to some event preceding the injury which he



can never remember in the ordinary way, as the event falls into the period of retrograde amnesia, and cannot be recovered even under barbiturate hypnosis. In 1934 I saw a patient in this hospital who, during the first week after recovering consciousness, had on many occasions the sudden vision of the huge tyre of a motor lorry bearing down on him while he threw up his arms unable to escape. He could always remember standing on a tramway island in Princes Street, but always failed to remember in the ordinary way this last item before his injury. Two other examples of this phenomenon are first of an army driver who, on recovering consciousness, had a clear vision of a brown horse, as in a cloud, galloping with its head up from right to left. There was no associated emotional reaction to this vision. He was never able to recall this last event before his accident, during which a runaway horse emerged from a side road, but his nurses said he had spoken of a horse during his period of confusion. The other case also concerns an army driver who was sitting next the driver at the time of an accident, when the steering mechanism of the car broke. About two weeks after the accident he had the first of six visions which were all the same and occurred within a period of a month. The vision consisted of the sudden appearance in his right visual field of a man's arms struggling with the steering wheel of a car. The vision lasted for a few seconds only, and used to come when he was sitting in an easy chair fully relaxed. The retrograde amnesia in his case was of twenty minutes duration and could not be reduced under barbiturate hypnosis.

These rare occurrences indicate a lower level of registration in which the process is cut short by the rapidly following concussion. It is of special interest that the visions are associated with little or no emotional feeling. They appear simply as events which evoke the patient's curiosity and only occur for a few weeks after the injury. They refer to incidents which would have stimulated the hypothalamic mechanism strongly had not the neuronal paralysis of concussion intervened presumably before the emotional reaction had time to develop sufficient strength for it to be subsequently recalled.

The retrograde amnesia associated with concussion is one of the best-known phenomena observed after head injury. In accidental closed head injuries of sufficient severity to cause some period of post-traumatic amnesia, a period of retrograde amnesia, usually for a second or two only, is almost invariable and was recorded in 97 per cent. of 1000 cases of head injury of sufficient severity to cause loss of consciousness. This must surely mean that the registration of even the most dramatic events requires a second or two of time to open up neuronal circuits in such a way that they can be used for subsequent recall. Even an interval of a second's duration is a long time in nervous physiology if we remember that the delay at each synapse is less than one milli-second. It seems, therefore, for an observed event, to enter the sensorium in such a way as to be available

for future recall, requires either that a chain of several hundred neurones is set in activity, or perhaps that a smaller circuit system must be opened up many times before the impression remains for future recall.

It is noteworthy, however, that incidents preceding a severe head injury by perhaps two or three seconds are often subsequently remembered quite clearly, so it seems that registration occurs in the space of a few seconds, and is by then so firmly established that it can withstand the effect of the widespread extinction of cerebral activity caused by severe cerebral concussion. This short interval required for registration makes it unlikely that any process more complicated than the full registration of the incident is required to make it available for future recall.

The study, however, of the effects of concussion on the memory of events preceding the injury leads to other questions of great interest. One is, for example, often impressed by the importance of the age of memory in relation to its recovery.

An excellent example of this phenomenon was provided by a Gullane greenkeeper, aged twenty-two, who was admitted to this hospital after a motor cycle accident in August 1933. Ten days after the accident he was bright and appeared to be mentally alert. When questioned, however, he said the year was 1924, and that he lived in Jersey, but was a schoolboy at Bushey in Herefordshire. This information proved to be correct for 1924, but since then he had been in Australia for five years, and a greenkeeper at Gullane Golf Club for two years. Two weeks after the injury he was orientated for time and place, could repeat the name, address and flower test with one error after two minutes, and repeated eight digits correctly. He could now remember returning from Australia two years previously, knew that he lived at Gullane, but could remember next to nothing of his work and life during these two years and did not know his Gullane address. He left hospital three weeks after his injury but subsequently had complete amnesia for all his stay in hospital, his first memory being of leaving hospital. On returning home, however, he still could not remember his two years spent in Gullane and felt he had just returned from Australia. His retrograde amnesia, however, continued to shorten and two and a half months after the injury he remembered all events quite clearly up to within a few minutes of the accident occurring.

This slow shrinkage of the duration of retrograde amnesia is an almost constant characteristic of the recovery of mental functions after concussion, and must clearly depend on some fundamental fact regarding the physiology of remembering. This relative vulnerability of recent memory is well seen also in old age and in cases of Korsakoff's psychosis.

Further evidence regarding the relative vulnerability of recent memory is provided by study of the duration of retrograde amnesia, for there is no doubt that the permanent duration of retrograde

amnesia tends to be greater in the most severe injuries. Table I shows clearly that the cases with a long retrograde amnesia usually have also a long post-traumatic amnesia. It must also be stressed that many cases occur in which a long retrograde amnesia includes incidents of importance to the individual which would otherwise be remembered without difficulty (Russell and Nathan, 1946).

TABLE I  
*Comparison Between the Duration of Retrograde and  
Post-traumatic Amnesia*

Duration of Post-traumatic Amnesia.	Duration of Retrograde Amnesia.	
	Under One Minute (107 Cases).	Over Thirty Minutes (35 Cases).
Under 24 hours . . .	79	2
Over 24 hours . . .	28	33

Knowledge acquired shortly before a severe head injury may be lost. A young child may lose half of her limited vocabulary, while a soldier may forget all he learned at a signalling course he attended just prior to his injury.

All these examples indicate that recent memories are relatively much more vulnerable than remote memories, irrespective of their importance to the individual. The interesting suggestion emerges that memories become strengthened by the passage of time irrespective of their importance to the individual. If we choose to think back to some of our earliest memories we can always think of some further incident of no importance which we have never consciously recalled for perhaps twenty years. We may also today recognise a road we travelled perhaps only once many years ago without ever thinking of it in the interval. It is hard to believe that the original neuronal circuits opened up by the remembered incident would survive had they been lying dormant all these years, and I would put forward for your consideration the possibility that such a neuronal circuit is kept alive and strengthened by the spontaneous activity of the neurones concerned.

It has sometimes been thought that forgotten memories are suppressed for some psychological reason. This must play a part in the mental behaviour of the hysteric, but this view is clearly absurd for the average person. There seems to be a large element of chance regarding which incidents are retained and available for future recall. The unusual event is easily remembered perhaps because it opens up an unusual neuronal pattern, but the preservation of even this incident depends to some extent on it remaining isolated. The first surgical operation we ever saw must have remained a life-long memory had it been the only one, but how many of us can remember this experience

now? The neuronal pattern involved in witnessing a surgical operation has been so much used that most of us have largely or entirely lost the recollection of that first adventure into the operating theatre. It seems, therefore, that an event to be easily remembered, must not only open up a little used circuit, but for its good retention the established circuit or engram must to some extent remain undisturbed by other similar events competing for the same neuronal patterns. On the basis of the hypothesis just put forward competition for use of one neuronal pattern will disturb the automatic strengthening of the original circuit however vivid the original experience may have been.

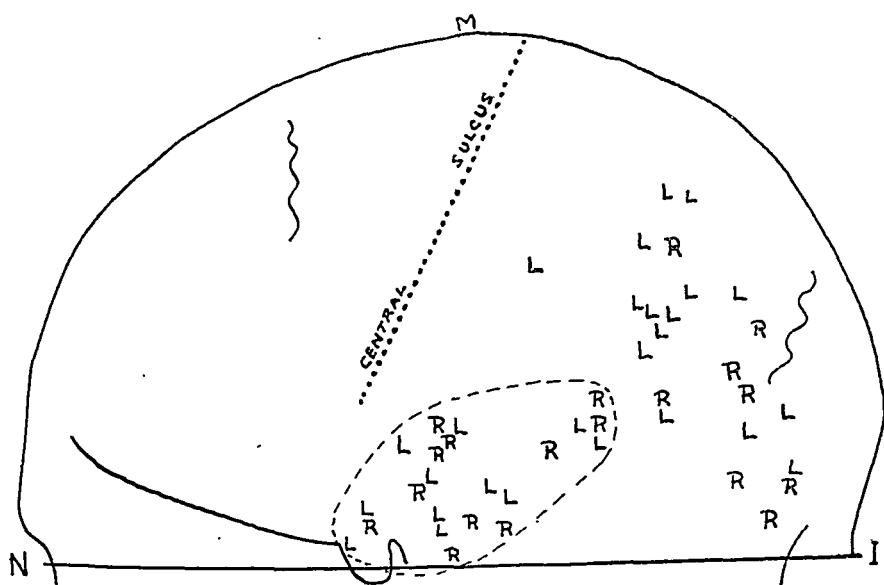


FIG. 1.—The site of the brain wounds studied of the right (R) and left (L) cerebral hemispheres, which all led to permanent damage to one optic radiation without injury to the sensori-motor system.

In what region of the brain then are these neuronal patterns opened up which record events and make them available for recall? Many workers have maintained that all parts of both cerebral hemispheres are concerned with memory and this may to some extent be true. On the other hand it is well known that either the whole of the right hemisphere or both pre-frontal lobes can be removed without any gross or constant loss of memory resulting. On the other hand severe injury to the dominant left hemisphere in its posterior part usually leads not only to aphasia but also to gross loss of memory and mental deterioration.

The study of the duration of amnesia in focal brain wounds throws further light on this matter. In a group of 250 cases of gun-shot wounds of the brain which penetrated the cerebrum for a distance of over 3 cms. there were 56 in which there was no amnesia relative

to the incident. There were a number of frontal, Rolandic, anterior temporal and posterior occipital wounds in this group, and some of the right parieto-temporal region, but there seemed to be a lack of wounds of the left posterior parieto-temporal region in which there was no amnesia.

More detailed evidence regarding this is provided by comparing wounds which injured the optic radiations on the right and left sides of the brain. Fig. 1 gives the site of wounds of this type. The criteria used for inclusion in this group are that the wound damaged the optic radiation but caused no pronounced permanent loss of sensation or weakness of the limbs of the contralateral side.

TABLE II

*Duration of Amnesia in Cases Charted on Fig. 1. Comparison Between Wounds of the Left and Right Side of the Brain*

Duration of Post-traumatic Amnesia (45 Cases).					
Side of Wound.	Nil.	< 1 hour.	< 24 hours.	> 24 hours.	Total Cases.
Right . . . .	7	5	1	6	19
Left . . . .	2	2	3	19	26

TABLE III

*Duration of Amnesia in Cases Charted Within the Dotted Line on Fig. 1. Comparison Between Wounds of the Right and Left Side of the Brain*

Duration of Post-traumatic Amnesia (22 Cases).					
Side of Wound.	Nil.	< 1 hour.	< 24 hours.	> 24 hours.	Total Cases.
Right . . . .	6	2	1	2	11
Left . . . .	1	...	1	9	11

Wounds penetrating the skull within 5 cms. of the midline are excluded in order to avoid most of the calcarine wounds. In all other respects the cases are unselected. This figure charts the site of wounding in 45 cases, 19 to the right side and 26 to the left side of the brain. The method of charting is by measurement of the site of the wound from skull X-rays according to a method described elsewhere (Russell, 1947). In Table II the prolonged amnesia commonly observed in wounds of this part of the left cerebral hemisphere is clearly shown. This contrast between the two hemispheres is even more striking in Table III which charts the wounds which penetrated straight in to the brain over the anterior part of the optic radiation. Though the number of cases in this group is small I am told that the difference between right and left is highly significant from the statisticians' calculations.

An interesting point emerges from these tables for if the cases in Table III are subtracted from those in Table II the resulting table shows no significant difference between right and left. The statistical significance therefore of Table II depends on it containing the cases charted in Table III. Further we have failed to find evidence of any difference as regards amnesia between right and left sides wounds in other parts of the brain, but this matter will be analysed more accurately at a later date.

These observations do not of course mean that the cortex overlying the anterior part of the optic radiation is a memory centre and indeed there are cases of cortical injury here without amnesia. All these wounds penetrated the white matter far enough to damage the optic radiation and presumably injured association paths between parietal, temporal and occipital lobes.

They do, however, strongly suggest that the white matter in this situation normally plays an essential part in the establishment of those neuronal circuits which are established by current events in such a way that they can be subsequently recalled to memory.

One must of course distinguish between this disturbance of current recording and any permanent loss of remote or recent memory, and I am not yet able to give you information regarding the permanent effect on memory of wounds in this situation. There was, however, in most of these left temporal wounds some persistent aphasia in which difficulty in finding the right word was usually a feature, and it should be noted that difficulty in finding words is a form of remote memory loss. All these patients were of course severely aphasic immediately after wounding, and were often reported to be conscious, but there is no association of early aphasia and long amnesia in wounds elsewhere in the dominant hemisphere. It is only the dysphasic cases who have wounds in this situation which show almost always this long amnesia after injury.

These observations indicate the need to study disease of the dominant hemisphere in a fuller manner than is provided simply by observing the effects on the speech mechanism. The pattern of human behaviour, memory and speech are all so closely linked that the study of aphasia alone is apt to be misleading.

I am particularly indebted to Dr R. B. Fisher for his statistical analysis of the tables.

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# BLOOD CHANGES IN THE AGED \*

## PART III

By OSCAR OLBRICH, M.D., Ph.D., F.R.C.P.E.

*From the Biochemical Laboratory, Royal Infirmary, Edinburgh and  
Queensberry House Hospital, Edinburgh*

*(Continued from p. 656)*

### PLASMA PROTEINS

THE estimation of the plasma proteins has been carried out in 78 old subjects, of whom 37 were males and 41 females. They were grouped according to age in three decades and according to sex. The average value for all subjects was found to be 5.701 gm. per cent. with a standard deviation of 0.606 gm. per cent. The range was 4.02-7.14 gm. per cent. With advancing years a slight decrease of the plasma protein content was distinctly noticeable in both sexes. A difference was also noted between the sexes, the mean value for the females being greater in all three age groups examined; this difference is statistically significant, being 2.74 times its standard error for the means of all ages. The difference arises mainly in the globulin component. Myers and Muntwyler (1940) reviewed the chemical changes in the blood and found a somewhat higher total protein content in females in the young.

Our figures also suggest a similar but smaller difference between the sexes in the albumin component; although the difference is found in all age groups, it is less than the amount required for definite statistical significance. As regards the fibrinogen component, the difference between the sexes is negligible.

Compared with our findings, the values reported on younger subjects by 32 investigators in the last 20 years (*see* Appendix V of the Medical Research Council Hæmoglobin Committee's Report) are consistently higher. The observations on serum protein (*ibid.*) are reproduced in Table XV for comparison with our Table XIII. The values in Table XV were derived from a group of 353 "unselected blood donors," nearly all below 60 years of age. In these observations no significant difference between the sexes was found, and also there was no clear evidence of correlation with age.

As regards age, it is clear that the values for serum protein in Table XIII do not form a continuous series with those of Table XV. The values for the "old people" are significantly lower than those for the "blood donors." The difference does not appear to be due to age only, as is seen from the last age group in Table XV. It is very probable that the "blood donors" of advancing years, say those over

\* Aided by a grant from the Medical Research Council.

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TABLE XIII

Sex.	No. of Observations.	Mean Values.					Standard Deviations.				
		A.	G.	F.	S.	P.	A.	G.	F.	S.	P.
Male .	37	3.185	1.965	0.364	5.15	5.514	0.408	0.455	0.090	0.584	0.597
Female .	41	3.304	2.207	0.359	5.511	5.869	0.435	0.570	0.085	0.562	0.593
Male + Female	78	3.247	2.092	0.361	5.340	5.701	0.417	0.522	0.0856	0.597	0.606

A = Albumin.

F = Fibrinogen.

G = Globulin.

S = Serum protein = A + G.

P = Plasma protein = A + G + F.

TABLE XIV

*Differences of Mean Values (Female Minus Male)*

Age.	A.	G.	F.	S.	P.
61-69 . . .	-0.09	0.48	-0.003	0.38	0.38
70-79 . . .	0.26	0	-0.022	0.26	0.24
80-98 . . .	0.09	0.56	0.021	0.65	0.68
All ages . . .	0.12 1.26	0.34 2.91	0.005 0.25	0.36 2.74	0.355 = Difference 2.64 = <i>t</i> ("Student's ratio")

A value of  $t > 2$  may be taken as indicating that the corresponding difference is statistically significant. There is a probability of 0.05 that a value as great as 2 should arise by chance.

A = Albumin.

F = Fibrinogen.

G = Globulin.

S = Serum protein = A + G.

P = Plasma protein = A + G + F.

TABLE XV

*Level of Serum Protein in a Group of Unselected Blood Donors*  
(Figures taken from Appendix 5 to the Hb. Report)

Age.	Number of Observations.	Mean Value.	Range.	Standard Deviation.
Under 20 . . .	9	6.757	6.35-7.22	0.3410
20-29 . . .	73	6.579	5.56-7.47	0.4023
30-39 . . .	123	6.603	5.58-7.45	0.4252
40-49 . . .	82	6.517	5.63-7.59	0.3814
50-59 . . .	48	6.487	5.74-7.06	0.3419
60+ . . .	9	6.572	6.17-6.97	0.2422
	<u>364</u>			
Males . . .	163	6.570	5.63-7.59	0.3886
Females . . .	190	6.552	5.56-7.65	0.4077
All . . .	<u>353</u>	6.560	5.56-7.65	0.3991

50, were a highly self-selected group of active and healthy people and by no means characteristic of elderly people generally, and certainly not comparable with the inmates of Queensberry House. Moreover, the small sample of 9 old "blood donors" cannot be considered representative.

The coefficients of variation found by us are very large compared with those noticed in the Report of the Hæmoglobin Committee. This indicates that, quite apart from the possible progressive change of the mean value with increasing age, there is a much greater variability in the older population. Table XIII strongly suggests a progressive decrease of the serum protein value with advancing years; in view, however, of the wide variability the decrease is too small to be considered statistically significant, and more extensive data would be necessary to establish it.

It will be seen, however, that the same apparent decrease is observed in the figures for the sexes separately; and the suggestion of decrease with age is also found in the albumin and globulin figures, especially if those for ages over 60 and over 80 are compared.

The persons from whom blood was taken for the purpose of our investigations were fasting and in bed, and it might be that the lower protein values obtained are partly due to posture. According to Lange (1946) the influence of the posture of the person from whom the blood is taken is of dominating importance. He found an average increase in protein concentration from recumbent to walking position of approximately 8 per cent. and from recumbent to standing position 14 per cent. He states also that this increase may be as high as 20 per cent. This phenomenon is explained by Lange by the altered hydrostatic pressure in upright position, which leads to an increased filtration of fluid from vessels to tissue. He examined 46 "normal-protein" patients when lying in bed, and found the average protein concentration to be approximately 7.45 per cent., with a range of 8.86-6.30. The average protein content in the recumbent patient was 6.88 per cent., and a still lower average figure of 6.62 per cent. was found in 8 normal male individuals after lying in a horizontal position for half an hour or more.

Unfortunately Lange did not investigate the different protein fractions. It would be of interest to see which fraction changes with a change of posture.

With regard to protein fractions, comparison may be made with the figures of Trevorrow *et al.* (1942), who investigated 547 healthy persons up to 40 years of age and obtained the following results:—

Albumin.—A mean concentration of 4.6 gm. per cent., with a range of 5.65-3.3 gm. per cent.

Globulin.—A mean concentration of 2.0 gm. per cent., with a range of 1.32-3.79 gm. per cent.

Fibrinogen.—A mean concentration of 0.25 gm. per cent., with a range of 0.38-0.19 per cent.

It appears to us that the albumin fraction is most affected in the aged. The mean concentration of globulin obtained by us is approximately identical with that found by Trevorrow. The fibrinogen fraction does not show any quantitative change in the aged, and its production by the liver in the aged is not impaired.

The three protein fractions vary independently in normal persons.

The production of the plasma proteins depends on exogenous and endogenous sources. The exogenous source is the food protein, and it has been shown by Whipple (1940) that not only quantitative but also qualitative feeding is of importance. Certain amino acids are essential for plasma protein formation.

Physiological variations in the plasma protein content have been reported due to food or fluid intake (Adler, 1918), but these do not exceed 10 per cent. This dependence on food intake is also pointed out in the Medical Research Council's Hæmoglobin Report, where a comparison between the plasma proteins of civilian blood donors and of a group of Canadian soldiers receiving more protein per day shows a similar advantage of the high protein intake.

The concentration of the plasma proteins may vary not only with age and sex but also with feeding. A dietary survey, therefore, has been carried out at Queensberry House and the daily amino acid intake calculated. This survey shows that the protein intake, including first-class protein, is practically identical with that for the whole population at the present time.

It is conceivable that with increasing age and equal protein intake, the absorption from the alimentary canal is diminished or the formation of the plasma proteins decreased.

Another possibility is that the endothelial permeability might be lower with advancing years, for any change in endothelial permeability influences the plasma protein concentration (Wiener and Wiener, 1930).

The endogenous source of the plasma protein is the body protein reserve, which might play a part in maintaining the normal level. This body protein reserve might be influenced by the preceding nutritional history of the subject investigated. The amino acid supply from the alimentary canal, the body protein reserve and the demand for protein within the body "are in a dynamic equilibrium" (Madden and Whipple, 1940). It might conceivably be that there is some disturbance of this dynamic equilibrium between the amino acids, the plasma protein and the "labile reserve" protein.

#### NON-PROTEIN NITROGEN

In 96 cases investigated for non-protein nitrogen an average of 37 mgm. per cent. has been found for both sexes, with a range of 22·4-54·32. The 44 males show an average value of  $38·5 \pm 1·25$ , with a range of 22·4-52·08, whereas the 52 females show an average of  $35·7 \pm 0·81$ , with a range of 22·96-54·32.

There is a steady increase of the non-protein nitrogen with advancing years, not only in the males but also in the females.

TABLE XV—B  
*Non-Protein Nitrogen in Mgm. Per Cent.*

Age.	Sex.	Number of Observations.	Mean Value with Standard Error.	Standard Deviation = $\sigma$ .	Coefficient of Variation as Per Cent.	Range.
89-80 .	Male	11	40.3 $\pm$ 2.03	6.7	16.25	30.8 -49.28
79-70 .	Male	24	39.1 $\pm$ 2.0	9.6	24.5	22.4 -52.08
69-60 .	Male	9	35.1 $\pm$ 1.51	4.54	12.9	28.0 -42.56
All .	Male	44	38.5 $\pm$ 1.25	8.26	21.45	22.4 -52.08
99-90 .	Female	6	38.66 $\pm$ 3.69	9.06	23.43	28.56-54.32
89-80 .	Female	13	37.08 $\pm$ 1.61	5.7	15.37	22.96-45.08
79-70 .	Female	22	35.05 $\pm$ 1.19	5.62	16.03	24.08-48.72
69-60 .	Female	9	33.5 $\pm$ 1.45	4.34	12.9	28.84-41.16
59-50 .	Female	2	35.56 $\pm$ 0.84	1.18	3.34	24.72-36.4
All .	Female	52	35.7 $\pm$ 0.81	5.85	16.38	22.96-54.32
All .	Male and Female	96	37.03 $\pm$ 0.69	6.71	18.1	22.4 -54.32

The male population shows higher values.

There is an increase with advancing years but the "norm" is in the range of the "norm" of the population.

### THE BLOOD SEDIMENTATION RATE

The blood sedimentation rate of 67 old subjects has been investigated by the Westergreen method. The group consisted of 34 males and 33 females. From the clinical point of view no gross lesions could be detected in the subjects apart from those caused by age, so that any abnormalities due to infective processes were excluded.

The subjects of both sexes showed an increased sedimentation rate of 11.9 mm.  $\pm$  0.9 with a standard deviation of 8.06. There is a suggestion of a sex difference, but it is on the whole, of doubtful significance. The tendency to an increase in the sinking velocity with advancing years is noticeable in every decade compared with seventh decade as a base line, but the increase is not progressive in the higher age groups; this applies to both sexes. The coefficients of variation indicate the wide variability of the sedimentation rate in all decades and in both sexes. Generally it might be concluded that the sedimentation rate increases with advancing years within the limits of 9.0-14 mm. in the first hour.

These findings are merely a confirmation of those of the majority of investigations concerned with the measurement of the sinking velocity in the aged. Loew-Beer (1929) observed the blood sedimentation rate in 429 persons and found an average value of 10 mm. in the first hour in males of the sixth decade, and 12 mm. in the females, whereas in the age group of 60-70 he found 14 mm.

for the males and 17 mm. for the females. Isaacs (1943) found not only an increased blood sedimentation rate, and this more marked in the females, but states that the rate is more rapid in the second hour. Westergreen (1924), quoting Plant, repeats his statement of increased blood sedimentation rate in the aged, relating it to vascular degeneration. Katz and Lefkowitz (1928) in their extensive survey relate the increased blood sedimentation rate in the aged to the increase of cholesterol in the blood of arterio-sclerotics. Müller-Deham (1937) relates the increased blood sedimentation rate in senility to a coarser dispersion of the colloids and increased amounts of fibrinogen. Reference has been made here only to those investigators who used the Westergreen method, although others, using different methods, have obtained similar results.

TABLE XVI  
*Blood Sedimentation Rate*

Sex.	Age.	Number of Observations.	Mean Value with Standard Error.	Standard Deviation = $\sigma$ .	Coefficient of Variation as Per Cent.	Range.
Male . .	88-60	34	$12.1 \pm 1.53$	8.94	73.8	2-37
Female . .	98-60	33	$11.7 \pm 1.26$	7.21	61.6	2-27
Male+Female	98-80	18	$10.5 \pm 1.7$	7.61	72.47	2-27
Male+Female	79-70	33	$14.0 \pm 1.5$	8.88	63.4	2-37
Male+Female	69-60	16	$9.2 \pm 1.5$	6.16	66.95	2-24
Male+Female	All	67	$11.9 \pm 0.9$	8.06	67.72	2-37

All investigators agree concerning the difficulty of establishing the standard of "normal" in the aged, as any septic focus, without clinical manifestations, increases the sinking velocity, and minor infections appear to have a greater effect on the sedimentation rate in the aged than in the young. This may be an important contributory factor both to the increased mean values for the sedimentation rate in old age and to the markedly greater variability. Insomuch as the greater effect of minor infections and their more frequent occurrence are "normal" concomitants of the ageing process, the figures presented in this paper may be accepted, though with reserve, as applying to "normal" old people.

The wide scatter of the figures for the blood sedimentation rate in these cases, and the fact that simultaneous determinations of the plasma protein fractions had been made, suggests that the data might usefully be employed in investigating the correlation between the sedimentation rate and the plasma proteins.

Ninety-seven subjects, on whose blood the sedimentation rate and plasma proteins had been determined, were classified according to the sedimentation rate irrespective of their clinical condition. Within

each group so obtained, the mean values for plasma albumin, globulin and fibrinogen were then calculated.

It is evident from Table XVII that increase in sedimentation rate is correlated with increase in plasma fibrinogen and globulin but, though less clearly, with decrease in plasma albumin. The table suggests that the sedimentation rate is governed (so far as the plasma proteins are concerned) by the resultant of an inhibitory effect on the part of the albumin and a stimulatory effect on the part of the fibrinogen and other globulins. It is the balance between the various protein fractions which counts, and not the total concentration of protein in the plasma, or even the concentration of any one protein fraction.

TABLE XVII

*The Protein Fractions in Correlation to Blood Sedimentation Rates*

	Normal.									
	1-5	5-10	10-15	15-20	20-25	25-30	30-35	35-40	40-45	45-50
Blood sedimentation rate										
Total protein	5.44	5.45	5.57	5.85	5.76	5.89	6.00	6.02	5.77	6.52
Albumin	3.18	3.22	3.32	3.37	3.32	3.29	3.00	3.12	2.95	2.86
Globulin	1.94	1.88	1.90	2.09	2.06	2.23	2.57	2.61	3.34	3.55
Fibrinogen	324	337	339	290	383	384	428	393	325	485 in mgm.

Ninety-seven subjects were investigated with regard to their blood sedimentation rate and corresponding total protein, and albumin, globulin, fibrinogen. No account was taken of their clinical condition.

To determine more precisely the effects of the various protein fractions and their relative importance, the correlation coefficients were calculated, with their standard errors. For this purpose the data from individual cases were used, and not the mean values of Tables XIII and XVI. The values found were:—

Blood sedimentation rate and plasma albumin :  $-0.308 \pm 0.052$ .

(Coefficient =  $5.8 \times \text{S.E.}$ —statistically significant.)

Blood sedimentation rate and plasma globulin :  $+0.286 \pm 0.093$ .

(Coefficient =  $3 \times \text{S.E.}$ —of doubtful significance.)

Blood sedimentation rate and plasma fibrinogen :  $+0.48 \pm 0.08$ .

(Coefficient =  $6 \times \text{S.E.}$ —clearly significant.)

It should not be concluded from these correlation coefficients that increases of plasma albumin, globulin, and fibrinogen have separately the indicated effect on the blood sedimentation rate. Their separate effects are obscured in this analysis by the possible inter-correlations of the protein fractions which have not been calculated. To clarify this point, it was necessary to use the method of multiple regression and to calculate the regression of the blood sedimentation rate on the three protein fractions. The regression of the logarithm of blood

sedimentation rate on A (albumin), G (globulin) and F (fibrinogen) was calculated by the method of least squares, and the result obtained was :—

$$\log \text{ blood sedimentation rate} = -0.2145 A + 0.668 G + 1.398 F.$$

(Logarithms were used because, while the distribution of blood sedimentation rate is very skew, that of log blood sedimentation rate is more symmetrical and is approximately normal, and because the theory underlying the use of regression equations of the above form presupposes that the variables which are being correlated are normally distributed. The distributions of A, G, and F are roughly normal.) This means that for every given value of A, G and F, the best estimate which can be made of blood sedimentation rate on the basis of the observations is the value determined by the above equation. The signs of the regression coefficients,  $-0.2145$ ,  $+0.688$  and  $+1.398$ ,

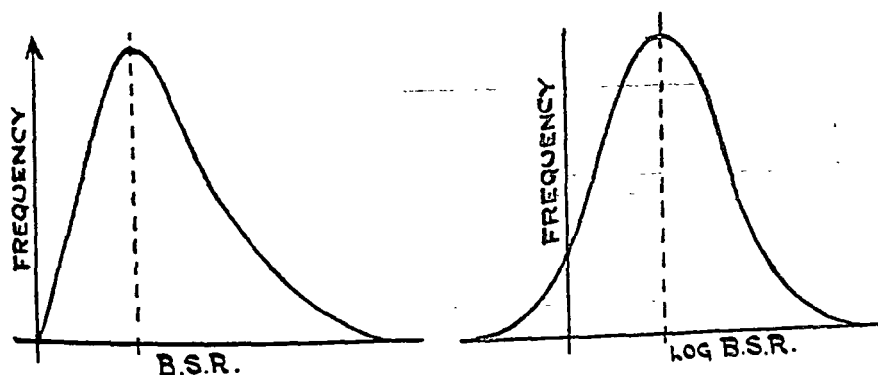


FIG. 6.

show that increase of globulin or fibrinogen separately increases the blood sedimentation rate, while increase of albumin separately decreases it.

The regression equation shows clearly that, *ceteris paribus*, the blood sedimentation rate is a function of the plasma proteins, although it does not exclude the possibility of other factors. Exchange experiments, however, while confirming this, suggest that the sedimentation rate is governed mainly, if not entirely, by the composition of the plasma.

In these experiments the sedimentation rate was determined for the blood of an aged person (A) and of a young person (Y), the two being, of course, of the same blood group. Meanwhile, further quantities of the same two bloods were centrifuged for 30 minutes at 3000 r.p.m., and the plasmas were exchanged. Mixing was accomplished by gentle shaking for 10 minutes, and the sedimentation rates were determined in the two mixtures :—

A cells + Y plasma :      Y cells + A plasma.



In both cases the rate observed was that characteristic of the plasma. A cells+Y plasma behaved like Y cells+Y plasma: Y cells+A plasma behaved like A cells+A plasma.

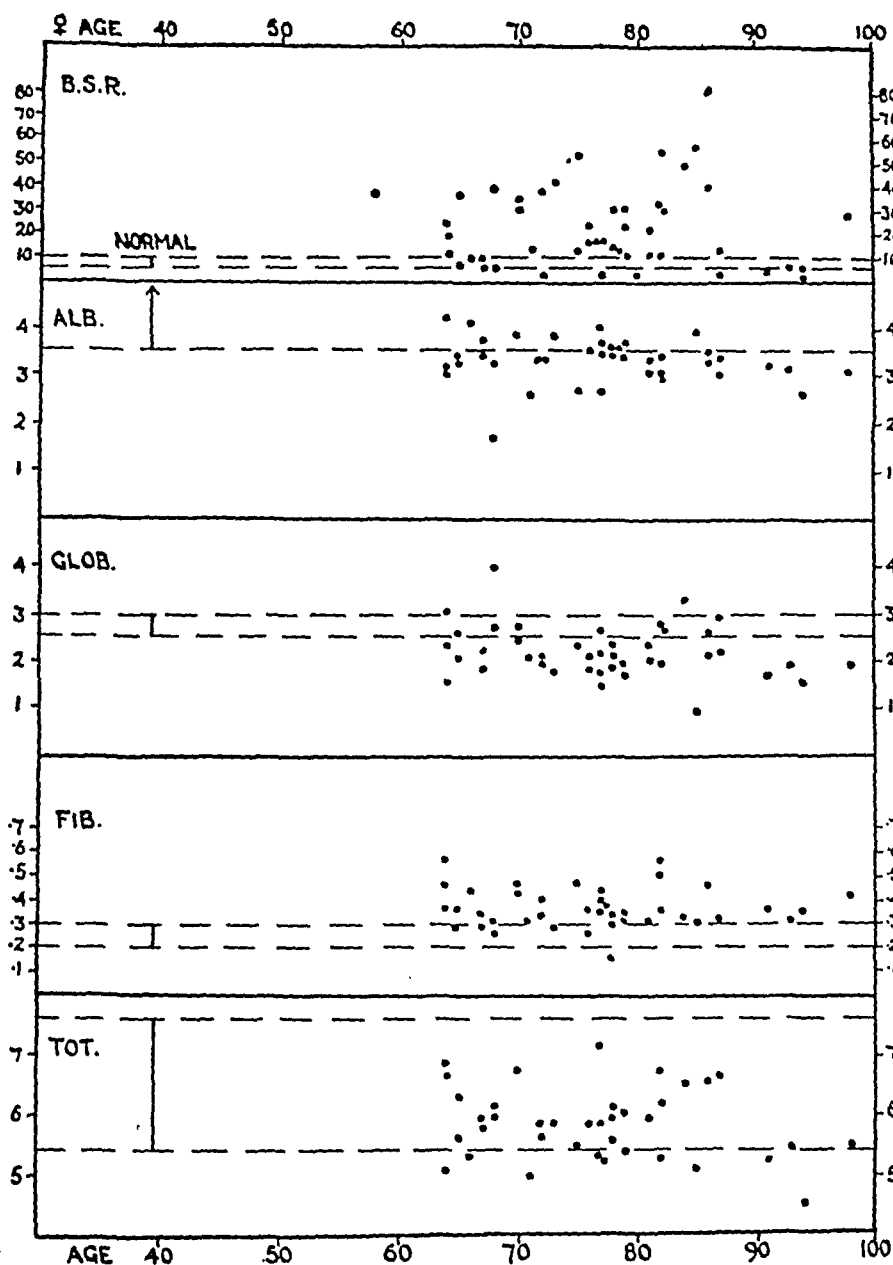


FIG. 7.—Blood sedimentation rate, albumin, globulin and fibrinogen and total protein scatter diagram in females.

A detailed discussion of the voluminous literature concerning the blood sedimentation rate and its relation to the plasma proteins would be out of place here, but one or two points deserve mention. Fahraeus has shown (1929) that the sedimentation rate depends on rouleaux formation, which in turn depends on the amount of fibrinogen present



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in the plasma. Addition of fibrinogen to the plasma increases rouleaux formation and the same happens if globulin is added to the plasma or if the albumin content of the plasma is reduced. As Fahreus says :

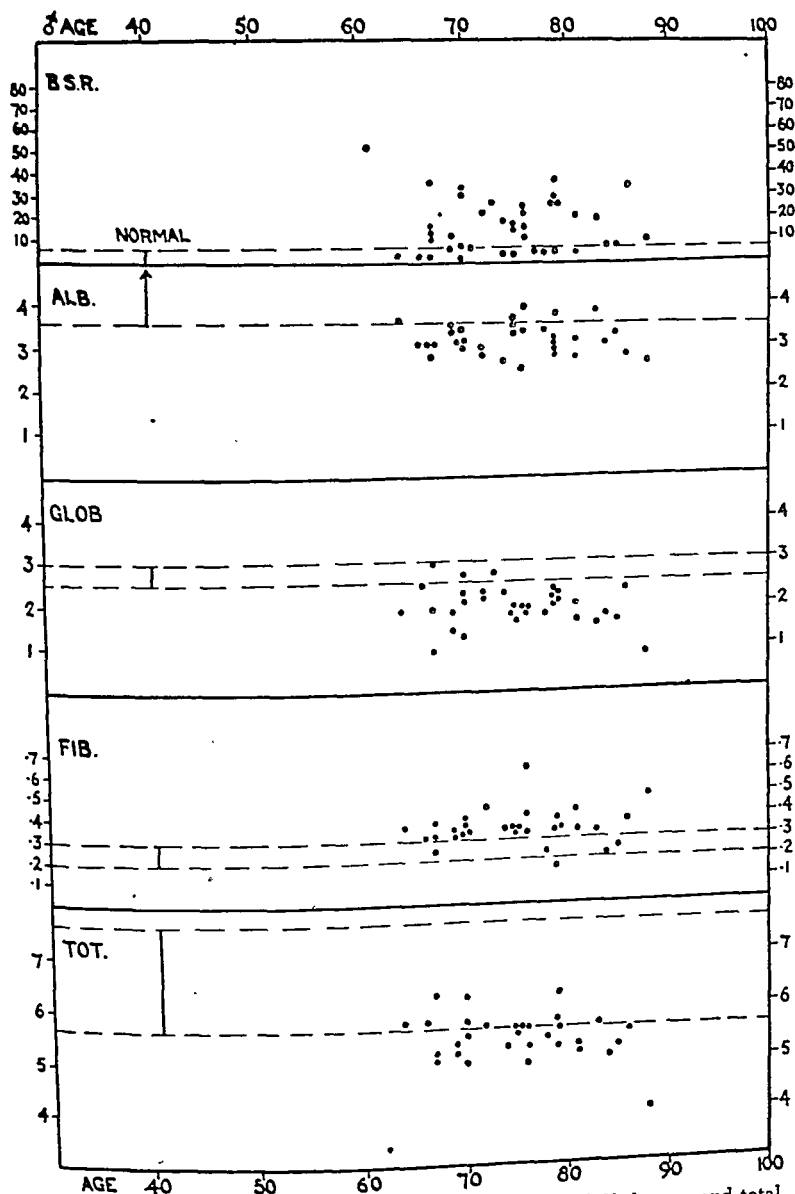


FIG. 8.—Blood sedimentation rate, albumin, globulin and fibrinogen and total protein scatter diagram in males.

"The plasma contains substances which are the vehicle of its aggregation capacity." The plasma, however, is not the only factor which influences rouleaux formation, on which the plasma lipoids, the blood gases as well as the proteins of the erythrocytes, all exert some effect. Gordon and Wardley (1943) express this balance by

the term of the "fastening" and "inhibiting" action of the protein fractions. Fibrinogen and euglobulin are the most active and the albumin (globo-glycoid) and nucleoproteins the most inhibitory, the other fractions being intermediate or neutral in action.

The sedimentation rate depends also on the precise technique and on the number, size and shape of the red cells. Of the technical factors, the anticoagulant used, the age of the blood sample, temperature, length of the sedimentation tube, bore and inclination of the tube and the recording method have been often and lengthily discussed elsewhere.

Some investigators, *e.g.* Aldred-Brown and Munro (1934, 1935); Ropes, Rossmeisl, Bauer (1939), have failed to find any correlation between the plasma proteins and the blood sedimentation rate, but the weight of evidence speaks against their findings.

The increased blood sedimentation rate in the aged does not depend on arteriosclerosis nor on coarser dispersion of colloids, but on the change of the plasma proteins.

### NUTRITION

For the purpose of investigation of the nutritional condition of the inmates of Queensberry House, the height and weight of each person was examined and a dietary survey carried out.

The average weight of the 163 cases investigated was approximately 58 kgm., this including persons aged 94. The average weight of the male group was 62.5 kgm. and of the female group 53 kgm. It is interesting to note that with advancing years the body weight decreases, as will be seen from the following table :—

Number.	Age.	Weight Kgm.	Height Metres.
Males :			
7 . . .	50-59	63.0	1.67
5 . . .	60-69	65.5	1.68
26 . . .	70-79	63.7	1.64
11 . . .	80-90	57.1	1.62
Females :			
19 . . .	50-59	60.78	1.54
22 . . .	60-69	52.03	1.56
43 . . .	70-79	52.16	1.53
30 . . .	80-94	49.60	1.52

The criteria of "normality" for the purpose of determining hæmoglobin levels, as postulated by the Hæmoglobin Committee of the Medical Research Council (1945) were fulfilled in the cases on whom our investigations were carried out, namely :—

1. A diet was given which was adequate in all respects.
2. There was no abnormality of gastric and intestinal function.
3. There was no increased demand for hæmopoietic factors which was not adequately covered by increased diet.
4. No change in the relative plasma volume could be detected.

The inmates consist of two groups of people. One group, which consists of about 40 persons, comes from the middle class and lives in a separate building, Queensberry Lodge. The other group comes from the artisan and lower middle class and lives in Queensberry House. It can be assumed that the nutritional condition of the first group was probably better during the whole lifetime than that of the second group.

The nutritional conditions in Queensberry House and Queensberry Lodge were in all respects normal for the purpose of our investigations. The catering provided was the same for the Lodge and for the House, although the actual preparation of the food was in different kitchens. Special care was taken that the food was appetising and varied, and there was a high standard of cooking in the Lodge. The nutritional value of the diet provided was, on the whole satisfactory, and the protein intake per day was reasonably good under wartime conditions.

The food provided for, and consumed by, the inmates of Queensberry Lodge and Queensberry House was as follows :—

	Daily Intake.			
	Queensberry Lodge.		Queensberry House.	
	Range.	Average.	Range.	Average.
Calories . . . .	1544-2130 cals.	1727 cals.	1628-2193 cals.	1876 cals.
Carbohydrate . . .	203-301 gm.	237 gm.	253-312 gm.	277 gm.
Protein . . . . .	55-72 "	62 "	46-81 "	62 "
Animal protein . . .	25-40 "	31 "	16-42 "	27 "
Fat . . . . .	50-71 "	59 "	47-64 "	56 "

The mineral intake in the food was found to be :—

	Queensberry Lodge.	Queensberry House.
Calcium . . . .	0.6 gm.	0.7 gm.
Iron . . . . .	11.0 mgm.	10.0 mgm.
Vitamin A . . . .	3282.0 I.U.	1183.0 I.U.
Thiamin . . . . .	0.9 mgm.	1.1 mgm.
Vitamin C . . . .	38.0 "	17.0 "
Riboflavine . . . .	1.5 "	1.0 "

In addition to the above, food was brought in by the patients' relatives and consumed by the patients as extras. This food was estimated as follows :—

	Queensberry Lodge.		Queensberry House.	
	Range.	Mean.	Range.	Mean.
Calories . . . . .	0-38-112 cals.	37.0 cals.	0-55-304 cals.	87.00 cals.
Carbohydrate . . . .	0- 2- 23 gm.	6.0 gm.	0- 9- 22 gm.	9.00 gm.
Protein . . . . .	0- 1- 3 "	0.6 "	0- 1- 13 "	3.00 "
Fat . . . . .	0- 1- 4 "	1.0 "	0- 1- 18 "	4.00 "
Calcium . . . . .	0- 3- 10 mgm.	3.0 mgm.	0- 9-365 mgm.	67.00 mgm.
Iron . . . . .	0- 0.4 "	0.2 "	0-0.2-0.9 "	0.30 "
Vitamin A . . . . .	0- 3- 89 I.U.	25.0 I.U.	0- 5-210 I.U.	92.00 I.U.
Thiamin . . . . .	0-12- 24 mgm.	9.0 mgm.	0-34-165 mgm.	0.04 mgm.
Riboflavine . . . . .	0- 6- 35 "	7.0 "	0-10-480 "	0.09 "

Taking as the average weight for both sexes the figure of 60 kgm., the protein intake is 1 gm. per kgm. body-weight; of this 1 gm. at least 50 per cent. is first-class protein.

In the consumed proteins the essential amino acids were calculated (except the extras) and these were found to be as follows :—

	Grams per Day.	
	Queensberry Lodge.	Queensberry House.
As protein . .	58·7	57·99
Arginine . .	2·84	2·81
Histidine . .	1·23	1·25
Lysine . .	2·88	2·84
Tyrosine . .	2·15	2·14
Tryptophan . .	0·71	0·73
Phenylalanine . .	2·97	1·89
Cystine . .	0·85	0·92
Methionine . .	1·51	1·01
Serine . .	1·54	1·52
Threonine . .	2·00	4·41
Leucine . .	4·85	4·87
Isoleucine . .	1·24	1·33
Valine . .	1·38	1·51
Glutamic acid . .	2·44	2·47
Aspartic acid . .	0·30	0·14
Glycine . .	0·74	0·48
Alanine . .	0·19	0·23
Proline . .	0·77	0·92
Hydroxyproline . .	0·03	0·01

It has been suggested that certain particular amino acids are necessary and desirable for stimulation of the production of plasma proteins. The need for cystine, for example, in the simultaneous regeneration of hæmoglobin and plasma protein after repeated hæmorrhage is implied by the results of Robscheit-Robbins *et al.* (1943).

The amount of essential amino acids consumed by the inmates of Queensberry House suggests that taking body weight into consideration the lower plasma protein value in these aged persons cannot be explained on the grounds of lack of amino acids or the intake of protein.

### SUMMARY AND CONCLUSIONS

1. The red cell population of the aged is distinctly different from that of the young. The quantitative data in regard to erythrocytes, hæmoglobin, colour index, total cell volume and mean corpuscular volume do not show any difference between young and old. The mean red cell diameter, however, is distinctly larger in the old, and the scatter as measured by the standard deviation or coefficient of variation is distinctly bigger.

2. The fragility of the red cell population as measured by the osmotic resistance to different concentrations of salt solution is distinctly increased in the old as compared with the young. By

plotting hæmolysis on probability paper, with a logarithmic base for the salt concentration, approximately straight parallel lines are obtained up to the 84 per cent. level of hæmolysis in old and young. A population of red cells whose resistance to hæmolysis was normally distributed would be represented by one straight line in the figure; the broken line obtained suggests the presence of a heterogenous population consisting of normo- and hyper-resistant cells, each component being approximately normally distributed, this statement applying to both old and young people.

The hyper-resistant cells from 84 per cent. up to the 100 per cent. level behave similarly in both old and young groups. The increased fragility in the aged, therefore, applies only to the so-called normo-resistant cells. By normo-resistant cells, a term arbitrarily chosen, we understand all the cells from 16 per cent. up to 84 per cent. Below 16 per cent. we have termed them hypo-resistant cells, and this avoids the difficulty which arises when using the old term "maximal and minimal resistance."

However, the variability of fragility is much greater in the old than in the young in both the normo- and hyper-resistant cells.

3. The blood sedimentation rate is increased in old age and is a function of the plasma proteins, other factors being equal. This is proved by the correlation coefficients and the regression equation; also by experiments involving equal volume exchange of plasma after half an hour's centrifuging. In these experiments:—

- (a) When cells of the young were suspended in plasma of the old, the blood sedimentation rate was increased as in the old.
- (b) When the red cells of the old were suspended in plasma of the young, the blood sedimentation rate was as that of the young.
- (c) When the red cells of an old person whose blood sedimentation rate was normal (between 2 and 10 mm./hr.) were suspended in a plasma of a young person whose blood sedimentation rate was normal, the blood sedimentation rate remained normal.
- (d) When the red cells of an old person were suspended in the plasma of a young person whose blood sedimentation rate was increased, the blood sedimentation rate remained increased.

These results also show that the plasma proteins behave differently in the aged.

4. The total white blood cells are present in equal numbers in the blood of the old and the young, but the differential count shows an entirely different behaviour as regards the number of lobes. The cells, as shown in the table, which contain more than 3 lobes are increased in number in relation to the total (100 per cent.); and at the same time the cytoplasm in the multilobulated cells contains fewer granules, in such a relation that the more lobes the nucleus has, the less granules the plasma contains. Cells were even seen



containing more than 5 lobes and containing scanty or no granules in the cytoplasm.

5. The non-protein nitrogen shows a distinct increase with advancing years, but not beyond the "normal" range.

6. From all the data with regard to the red and white cell population of the aged, we might venture the hypothesis—in view of their maintained numerical quantity but different qualitative behaviour—that the bone marrow produces in one time-unit a lesser amount of red cells and leucocytes. This means that the rate of production in the aged is diminished. At the same time, however, the rate of destruction is also diminished and a cell population is maintained probably for a longer time in the older person, but apparently of a different quality.

7. The nutritional condition of the subjects has been investigated, and it has been found that protein, fat, carbohydrate intake and total caloric intake is approximately the same as that of the general population, taking body weight into account.

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## SOME EDINBURGH MEDICAL MEN AT THE TIME OF THE RESURRECTIONISTS \*

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SOME time ago I was asked to give a paper to this combined meeting on some historical subject connected with the Edinburgh Medical School. Since you are to be guests at a performance of Bridie's "The Anatomist" tomorrow evening, it was suggested to me that I might speak of some of the medical men of Edinburgh at the time of the Resurrectionists. I hope that what I have to tell you tonight may be of some interest and may enable you to obtain some sort of background for a more complete enjoyment of the play. "The Anatomist" centres round the figure of Dr Robert Knox, one of our leading anatomists in the twenties of the last century, and he it was who gained an unwelcome notoriety by reason of his close association with Burke and Hare, the Edinburgh West Port murderers.

Before proceeding to discuss some of the leaders of Edinburgh medicine at the time of Knox and the Resurrectionists, may I be permitted to give a brief outline of the Resurrectionist movement in this country.

Prior to 1832, when the Anatomy Act was passed and the supply of anatomical material for dissection was regularised, there existed no legal means for the practical study of anatomy in Britain, save for the scanty and irregular material that was supplied by the gallows. Yet the law demanded that the surgeon possess a high degree of skill in his calling! How, then, was he to obtain this skill without regular dissection? The answer is that he obtained his material by illegal means, viz., rifling the graves of the newly-buried. To those individuals who opened graves and removed the corpses, the names of "Resurrectionists," "Resurrection-men" or "Sack-'em-up Men" were given.

With the rise of Edinburgh as a medical centre, in particular of its anatomical school under the two Monros, *primus* and *secundus*, and the later development of extra-mural anatomical teaching during the professorship of the incompetent *Monro tertius*, the Resurrectionists became busy both in and around the city and in other parts of Scotland. The Resurrectionists of Dublin also assisted the Edinburgh School and a regular traffic in corpses developed between the two cities (Ball, 1928). The first three decades of the nineteenth century mark the peak period of the resurrectionist movement. Public indignation, roused by the evidence revealed during the trial of Burke and Hare in 1828, effectively put a stop to resurrectioning in Scotland, but a Bill introduced into Parliament in 1829 and intended to free anatomists from the restrictions under which they laboured, was withdrawn.

\* Read at a Joint Meeting of the Tuberculosis Association and the Tuberculosis Society of Scotland held in Edinburgh on 16th July 1947.

Only in 1832, after the Anatomy Act was finally passed did resurrectionism become, for all practical purposes, extinct in Britain.

These resurrectionists comprised two groups of men. The first group was composed mainly of anatomists, surgeons, physicians and medical students, who, though their activities were illegal, were largely animated by a desire to advance science. As members of this group we might cite such men as the immortal John Hunter, Robert Liston and Sir Charles Bell.

The second group consisted of low fellows, whom Sir Astley Cooper described as "the lowest dregs of degradation" (Ball, 1928), and whose activities were pursued solely for financial gain, who stopped at nothing to achieve these ends, and whose patron was ever he with the most liberal purse. Some of the Edinburgh members of this group were well-known characters locally and rejoiced under such names as "Merry Andrew," the "Stupe" and the "Spune" (Macgregor, 1884).

As extra-mural teachers of anatomy and surgery quickly increased in numbers during the first quarter of the last century, competition for "subjects" became acute, and the rival gangs of resurrectionists had many encounters, often bloody.

The general public gradually became cognisant of the activities of these intruders, and began to take measures to circumvent them. Guarded graves, such as still may be seen in Greyfriars' Churchyard here, and watchers over the graves were both tried but with varying success. Too often whisky, darkness and the eerie surroundings of the graveyard proved too much for the watchers who deserted their posts leaving the coast clear for the "thieves of the night."

Burke and Hare appeared on the scene in the winter of 1827, but, having no stomach for body-snatching, they resorted to cold, calculated murder—one of the fine arts of de Quincey. The method adopted by this couple was to render their victims drunk with whisky, then to compress their mouths and nostrils, or else to smother them as they lay in their drunken sleep. By such means, some sixteen corpses of murdered folk were provided by Burke and Hare for Dr Knox before that infamous pair were arrested in November 1828. The subsequent events of the trial of this couple are well known. Hare escaped the hangman's loop by turning King's Evidence, while Burke paid the supreme penalty by public hanging on 29th January 1829. The day following, a public lecture and demonstration was given on Burke's brain—an event which nearly resulted in serious rioting in the City. On the 31st January, the general public were permitted to view Burke's body and Sir Walter Scott wrote in his *Journal* that, "all the world flock to see him." After this exhibition, the body was further dissected and preserved for future lectures. Burke's skeleton now rests in the Museum of the Anatomy Department of our University here.

Might I remind you that during the first thirty years of the nineteenth century, Edinburgh was not only the world centre of

medical education, but this period also marked the culmination of her intellectual glory (Gillies, 1886). It was the period of the philosophy of Dugald Stewart, of the physical researches of Playfair, Leslie and Hope, of the portraiture of Raeburn, of the immortal writings of Sir Walter Scott, of the Bar resplendent in Jeffrey, Cockburn and Moncrieff. In the twenties appeared the facile pens of John Wilson ("Christopher North") and John Gibson Lockhart. *The Edinburgh Review* exerted its all-powerful influence in literary criticism, while *Maga*, *Blackwood's Magazine*, and the publishing house of Constable were known to all.

The leaders of Edinburgh medicine at this time were men of powerful personality and forcible character and exerted their influence on medicine throughout the world.

The first who falls to be briefly mentioned is Alexander Monro, *tertius* (1773-1859). Appointed Professor of Anatomy at the University in 1798 as colleague and successor to his father, Monro *secundus*, he was indifferent to his students and careless, though he lacked neither ability nor accomplishments (Christison, 1885). Garrison (1929) refers to him as "the evergreen tertius." Small wonder, then, that he soon lost command over his class, though Christison admits Monro gave a very clear and complete course of lectures on anatomy.

Monro was one of the central figures in a most exciting afternoon in the history of anatomy. In the presence of a great concourse of local celebrities and students, he lectured on Burke's brain the day after the execution.

Monro practised as a physician, and this, combined with his ineptitude in teaching anatomy, contributed to the steady rise of the extra-mural anatomy teachers, and to the clamant necessity for instituting a Chair of Surgery within the University, since Monro's duties as Professor of Anatomy also included instruction in surgery, a subject which he dealt with in a most perfunctory manner in his lectures.

Such, then, was the way anatomy and surgery were taught in the University, and small wonder, therefore, that other, more striking figures appeared outside the sacred walls and began to teach these subjects.

One of these extra-mural teachers of anatomy and surgery who arose during the period under review was John Barclay (1758-1826). He had an active period of teaching extending from 1797-1825. Destined for the Church, for which he qualified after a distinguished academic career, he turned his attention to medicine and graduated M.D. at Edinburgh in 1796. After spending a year in London studying anatomy under Marshall, Barclay returned to Edinburgh and began to teach it privately. After a period of struggle, he gained official recognition as a teacher in 1804, and from that time his classes swelled rapidly in number, many students transferring their attendance from Monro to Barclay (Struthers, 1867).

Barclay was a clear and witty lecturer, holding the attention of his audience by the frequent use of apposite anecdote. His knowledge

of anatomy was profound, and he was often consulted by surgeons before they tackled some difficult or intricate operation (Struthers). His liberality was proverbial, and many a medical student had reason to be grateful for Barclay's generosity.

Comparative Anatomy was Barclay's special study, and he at one time petitioned the Town Council of Edinburgh to be made Professor of that subject in the University, but his petition failed. Nevertheless, he was largely instrumental in having established the Royal (Dick) Veterinary College here. He was not a prolific writer, but his works were of a high standard, and he retained to the end an early interest in philosophy. He retired from teaching in 1825, being succeeded by Knox, his assistant, and he died in 1826, bequeathing his excellent museum to the Royal College of Surgeons of Edinburgh.

Robert Knox (1791-1862) next must be mentioned. Dux of the Royal High School of Edinburgh, he entered the University and graduated M.D. there in 1814. After a period as military surgeon, he studied in Paris, absorbing the works of Bichat, Cuvier and St Hilaire. He then returned to Edinburgh, becoming assistant and then successor to Barclay.

Knox was an able and gifted teacher and investigator, gathering around him such men as (Sir) William Fergusson, Thomas Wharton Jones, John Goodsir and Thomas Hodgkin when students. He quickly made his mark and his anatomical lectures and demonstrations were sometimes attended by over 500 students in a year. To achieve his ambition to be the principal teacher of anatomy in Edinburgh, Knox stinted neither time, labour nor expense, and to ensure that his dissection tables were never bare, he was reckless of his own pocket, and in "one session he lost the almost incredible sum of £700 or £800 by 'subjects' alone" (Lonsdale, 1870). His tables as a consequence were always well furnished, and being no modest man, he openly declared that he could command subjects always—an unfortunate boast in view of later events (Roughead, 1921).

Knox's wit was caustic and egotistical, and his remarks on his fellow anatomists and surgeons openly critical. Socially he had little success, though it is said that he fascinated women. Physically he was unattractive, having lost the use of his left eye as a consequence of an attack of confluent smallpox in childhood.

Knox was at the very height of his fame when Burke and Hare were arrested in 1828. When the facts of the nefarious activities of these two scoundrels became public, Knox was at once the object of popular anger. His house was besieged by infuriated mobs and effigies of him were hung in various parts of the City. In spite of all this abuse, however, Knox preserved a rigid silence, even in the face of vituperative attacks in the press. Finally, a specially appointed committee, after enquiring into the relations which Knox bore to Burke and Hare, largely cleared him of blame—an opinion endorsed by Henry Cockburn (1856). Other contemporaries, such as Sir Walter

Scott, Christopher North and a medical colleague Sir Robert Christison, were gravely perturbed by his behaviour and passed censure on his actions in not inquiring as to the origin of his anatomical material. Generally speaking, taking Knox's position in relation to his times, he was no worse in his conduct than his fellow anatomists in Britain generally (Currie, 1933).

Knox's students were delighted with their idol's "acquittal" and presented him with a gold cup—an act *The Scotsman* (25th March 1829) described as "injudicious." But from that time the ability of Knox as teacher and investigator declined, and he left Edinburgh in 1844, dying in London in 1862.

Other anatomists of the period were Andrew Fyfe (died 1824), John Gordon (died 1818), David Craigie (died 1866), William Cullen (died 1828) and John Lizars (died 1860).

Turning now to the surgeons of the period, let us take a brief look at some of these men.

John Bell (1762-1820) was the older brother of Sir Charles Bell, with whom he was associated for a time in the teaching of anatomy in Edinburgh. John, however, forsook anatomy for surgery in 1799 (Struthers). He was a skilled draughtsman as well as an expert anatomist, and his *Engravings of the Bones, Muscles and Joints*, published in 1794, revealed one who had set out to help the surgeon in his figures. He was, in fact, the Father of Surgical Anatomy. Patients came to John Bell from all over Britain and even from the European Continent.

Bell had a high regard for the dignity of his profession, and spared no efforts to qualify himself both professionally and culturally. His library was a storehouse of the works of the masters, both of medicine and of the arts. The warmth of his temper, unfortunately, involved him in many disputes and his notorious quarrel with James Gregory was a long and bitter one. Both partisans wrote several volumes about it, Bell's main contribution being his "Letters on Professional Conduct and Manners; on the Education of a Surgeon, and the Duties and Qualifications of a Physician; Addressed to James Gregory, M.D." After a long peregrination on the continent, John Bell died at Rome in 1820.

Robert Liston (1794-1847), probably the original of Robert Louis Stevenson's Dr Macfarlane in *The Body Snatchers* (Guthrie, 1945), was at first the assistant to Barclay before striking out on his own as a teacher of anatomy during session 1818-19. He was an active resurrectionist as a student. A man of unusual initiative and considerable dexterity in operations, Liston rapidly became a well-known surgeon, but his uncompromising manner, together with a certain jealousy on the part of his seniors, involved him in many quarrels.

Liston's surgical publication of a series of cases of aneurysm in 1820 really set the seal to his reputation, and his further work on amputations and lithotomy added to his fame. He left Edinburgh in 1835 for London where he gained further renown by carrying out

what was generally considered to have been the first major operation under ether anæsthesia in this country, at University College Hospital in 1846. Recent research seems to point to the first operation under ether anæsthesia in Britain having been performed at the Dumfries and Galloway Infirmary at an even earlier date (Underwood, 1946).

Liston, in spite of his bluntness of manner, obtained his world-wide reputation by a high character and professional ability. He was suddenly cut off in his prime in 1847 when he died from an aortic aneurysm.

James Syme (1799-1870), the "Napoleon of Surgery" (Miles, 1918), and the father-in-law of Lord Lister, was one of the younger and abler surgeons of the period under review. As a youth of eighteen, he narrowly missed fame as a chemist by the discovery of the process of "waterproofing" cloth. As a pupil of Barclay and colleague of Liston, Syme early acquired a thorough knowledge of anatomy, but he ever regarded anatomy as a means to fitting himself for surgery. His early interest in bone and joint surgery established his reputation, but being unsuccessful in his application for the post of surgeon to the Royal Infirmary here in 1829, he set up his own hospital in which he taught clinical surgery, and which has been immortalised in "Rab and his Friends" (Brown, 1897). Syme in his later years looked back on these early days with pride, as he accomplished much during the life of that little hospital.

Syme was appointed Professor of Clinical Surgery in Edinburgh in 1833, and, save for a short period in London (1848), he held this chair till 1868, when he resigned following an apoplectic seizure. His *Principles of Surgery* is a masterpiece of clear exposition. It was said of Syme that "he never wastes a drop of blood or of ink," and as a surgeon "in all supreme, complete in every part" (Brown).

Other surgeons of the period were James Russell (1755-1836), the first Professor of Clinical Surgery in the University (1803)—"a somnolent lecturer, . . . yawning while he spoke, and continuing to speak while he yawned" (Christison, 1885), John Thomson (1765-1846), first Professor of Military Surgery in the University (1806); J. W. Turner (1790-1836) and Sir Charles Ballingall (1780-1855).

An extraordinary character of the times was James Hamilton (died 1839), the Professor of Midwifery from 1800 till his death. He was the acknowledged head of obstetrics in Scotland, and gave clinical instruction to his students in a lying-in hospital maintained at his own expense. After long efforts attempting to get midwifery made a compulsory subject in the medical curriculum, he finally succeeded in doing so in 1833 (Comrie, 1932).

Though generous and kindly both to his students and patients, Hamilton was a trenchant critic of his colleagues and always regarded himself as in the right (Christison). His legal actions against Hope and Gregory are well known to you all, and created great interest among the citizens of Edinburgh at the time.

Mention of Gregory brings me to the physicians, and who deserving



of mention first more than James Gregory himself? The successor of the great William Cullen, he was quite the most imposing figure, mentally and physically, among the medical brethren of the Edinburgh of his day. Rapidly achieving an extensive practice and wide popularity, and basing his therapeutic armamentarium on blood-letting, cold affusions, brisk purging and vomits of tartar emetic, he was, nevertheless, in advance of his time in many respects. Thus he taught how frequently rheumatism led to heart disease, and he urged a light diet in the early stages of pulmonary tuberculosis and a more liberal one during the chronic stages, and, of course, he achieved immortal fame by the invention of his celebrated powder.

Gregory's *Conspectus Medicinæ Theoreticæ* was a model of completeness and of classical elegance. It obtained instant and wide success, being adopted as a standard textbook at some German Universities (Christison). Gregory always lectured to his students wearing his three-cornered hat, while, when walking about the City he carried his stick military fashion over his shoulder. Forceful in action, he was fearless in speech, and his disputes with John Bell, the surgeon-anatomist, and James Hamilton have already been noticed.

Suffering much from attacks of pulmonary inflammation in his declining years, Gregory died from hydrothorax in 1821.

Our next physician is Andrew Duncan, senior (1744-1828)—“The Old Club-Maker” so-called from his activity and enthusiasm as a promotor of medical and social clubs. Professor of the Institutes of Medicine, he was an amiable old gentleman, behind the times in his lectures, from which his students learned little (Christison). He is deserving of notice for he advocated in 1798 in a Memorial presented to the Patrons of the University, the teaching of Medical Jurisprudence. This term comprehended both Medical Police or what we might now call Preventive Medicine, and Juridical Medicine which Duncan asserted was “the aggregate of all the information afforded by the different branches of medicine which is necessary for elucidating doubtful questions in courts of law.” Duncan also exerted himself greatly in obtaining Royal Charters for no fewer than four institutions, including the Royal Edinburgh Asylum for the Insane.

John Abercrombie (1780-1844) was a most successful physician in the City though he held no academic position. He gathered around him a group of apprentices, conducting what was in effect a private medical school. He divided the City into five districts and assigned patients in each of these to a certain number of his senior students. At the Royal Public Dispensary, of which he was physician, he organised a form of Polyclinic. He was an ardent pathologist and contributed much of value to the medical journals. Abercrombie was honoured by Oxford University and by Marischal College, Aberdeen, being appointed Lord Rector there. As a philosopher, Abercrombie's writings received favourable notice from contemporary reviewers. Sudden rupture of the heart caused his death in 1844.

In conclusion, we might mention James Home (1758-1842), Professor of Materia Medica (1798), and later of the Practice of Physic (1821); Andrew Combe (1797-1847), a pioneer in health education and somewhat addicted to phrenology; James Scarth Combe (1796-1883), a general practitioner of Leith, who gave the first description of a case, including post-mortem appearances, of pernicious anæmia; Sir Robert Christison (1792-1882), Professor of Medical Jurisprudence (1822) and later of Materia Medica (1832). A medical jurist of great merit, Christison made his early reputation by his work on toxicology and on bruising of the living body, the latter work carried out in connection with the Burke and Hare murder trial. His *Autobiography* published in 1885 is a rich source of information of the Edinburgh Medical School and its members during the period of his student and later life. For much of what I have told you this evening I am indebted to his reminiscences. Finally, William Pulteney Alison (1790-1859), who was the beloved teacher of William Stokes. Alison's work on infectious diseases and the influence of poverty and social conditions on the spread of disease contributed much to the framing of the Poor Law (Scotland) Act, 1845.

I am afraid that my sketch has been very scrappy and incomplete. There were so many worthies to choose from that I found difficulty in selecting those for special mention and those for passing over. However, I hope that I have been able to convey something of the spirit and endeavour of these men to whom we in Edinburgh owe so much.

To those of you who are especially interested in the history of medicine, you will find in Edinburgh a rich ground of tradition, while the museums, relics and graves of many notable medical men exist in various parts of the City.

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## NOTE

A QUARTERLY Meeting of the College was held on Tuesday, 3rd February, the President, Dr W. D. D. Small, C.B.E., in the Chair. Royal College of Physicians of Edinburgh Dr John Craig Rose Greig (Kirkcaldy), Dr Ian Nicoll Sutherland (Edinburgh), Dr Richard Oliver Gillhespy (Birmingham), Dr John George Macleod (Edinburgh), Dr Thomas Gow Brown (Hamilton) were introduced and took their seats as Fellows of the College.

Dr Eric Wilfred Frecker (Sydney, N.S.W.), Dr David Noble Dobbie (Bromley, Kent) and Dr Sarel Francois Oosthuizen (Pretoria, South Africa) were elected Fellows of the College.

Drs Joseph Gilley Dathan (Stoke-on-Trent), Selwyn Graham Nelson (Sydney, N.S.W.), Frederick John Booth (Brisbane, Queensland), Joseph Adler (Clarkston, Renfrewshire), John James Tillie (Edinburgh), William Ewan MacLean (Aviemore, Inverness-shire), James Leckie (Pitcaple, Aberdeenshire), Abdul Khair Shamsuddin Ahmed (Dacca, Bengal), Gerald Comay (Cape Town), William Ralph Nicholson Friel (Birmingham), Douglas Edmondston Ross (Edinburgh), Murdoch Beaton (Edinburgh), William Hugh Galloway (Edinburgh), Andrew Barry Hegarty (Edinburgh), Thomas Grahame Fox (N.Z. House, London), George Morrison Carstairs (Edinburgh), Elsie Craig Gibbons (Wellington, N.Z.), James Stanislaus Calnan (Eastbourne), Sujoy Bushan-Roy (Rangoon), Julius Buch (Johannesburg), Arnold Howard Banton (Edinburgh), Robert McKenzie Fulton (Edinburgh), John Norrie Swanson (Edinburgh), Petrus Jacobus Johannes Barnard (Gwelo, S. Rhodesia), Solomon Jacobson (Johannesburg), David Hazell Clark (Edinburgh), Marjory Anne Keith (Edinburgh) and Hilary Frances Hoyte Hamilton (London) were elected Members of the College.

## NEW BOOKS

*Irish Medical Directory, 1946-47.* Pp. 336. Dublin: Parkside Press. 1947. Price 15s. 6d.

The ninth edition of this Directory has now been expanded to cover the whole 32 counties and not merely the 26 of Eire. It contains notes on all medical practitioners in Ireland and, in addition, full details about hospitals and the staff. Two articles of interest are included, one on Penicillin by Ian Fraser, and one on the Sulphonamides in Surgery by William Devlin.

*Catalogue of Lewis's Medical, Scientific and Technical Lending Library—Supplement for 1944-46.* Pp. iv+176. London: Lewis's Library. 1947. Price 5s. net.

Lewis's Catalogue is a well-known and useful publication which gives details of all modern books in medicine and the allied sciences. The new supplement covers the years 1944-46. It is in two parts, the first an author index, the second a subject index classified under various branches of knowledge.

*English-Spanish Medical and Chemical Dictionary.* By MORRIS GOLDBERG. Pp. ix+692. London: McGraw-Hill Book Company. 1947. Price 50s.

This work contains Spanish equivalents for some 40,000 English words employed in Medicine, Chemistry and related sciences. In each case there is also a short

definition in Spanish of the English word. The author claims to have included more than 2000 new Spanish terms hitherto unrecorded in dictionaries.

The book is excellently produced, though the caution is given that the quality of materials used is governed by continued post-war shortages.

*Man Against Pain: The Epic of Anaesthesia.* By HOWARD R. RAPER, D.D.S. Pp. 236, with 22 illustrations. London: Victor Gollancz Ltd. 1947. Price 10s. 6d.

The title of this small compact volume is deceptive in that the prospective reader might think that here is another literary orgy of sentimentalised and over-dramatised medical history. He who ignores the outer cover, however, and reads on will be rewarded by the most entertaining factual record of the evolution of anaesthesia yet written. The author, a master of benevolent satire, covers the familiar matter from the earliest historical period until the present day in a style, reminiscent of Quentin Reynolds, which compels the reader to go on reading long after he ought to be in bed.

*Sensory Mechanisms of the Retina.* With an Appendix on Electoretinography. By RAGNAR GRANIT, M.D. Pp. xxiii+412, with 178 illustrations. London: Oxford University Press. 1947. Price 35s. net.

The study of the conduction mechanism of the retina and optic nerve has interested physiologists for many years and the modern development of refined and delicate electrical methods of research has enabled results hitherto unattainable to be achieved.

After an interesting and valuable historical introduction, the subject is dealt with in four sections of approximately five chapters each. The electrical signs of excitation and inhibition in the retina and optic nerve, the properties of the rods and cones, the properties of the photosensitive substances and the mechanism of excitation, and, lastly, colour reception, are discussed in the light of the results obtained by the electrophysiological approach.

Professor Granit has written a valuable book, breaking new ground. While it is clearly intended for physiologists who are experienced in the electrical measurement of nerve excitation and specially interested in the retina and optic nerve, it will also appeal to all who are interested in the mechanism of vision. It is freely illustrated by electoretinograms and graphs and completed by two appendices, an exhaustive list of literary references, and excellent author and subject indices.

*Law Relating to Hospitals and Kindred Institutions.* By S. R. SPELLER, LL.B. Pp. xxviii+400. London: H. K. Lewis & Co. 1947. Price 22s. 6d.

Several recent cases in the English Law Courts (*Gold v. Essex County Council*, *Collings v. Herts County Council*) have aroused wide interest in hospital and medical circles. Hitherto the decision in *Hillyer v. St Bartholomew Hospital* has been held to give immunity to hospital managements against action for mistakes or negligence of the qualified staffs. The case of *Gold* has thrown doubt on this. The author is an acknowledged authority on laws relating to hospitals, and the present book will fill the need which for long students of hospitals have felt for an up-to-date and reasonably comprehensive textbook on hospital law. While the introduction of the National Health Service Acts in England and Scotland will alter the relationships of the present voluntary hospitals to the community, the laws regarding injuries to patients by accident, negligence or incompetence, etc., still hold good. This aspect is thoroughly discussed. Too many professional administrators, doctors and matrons are apt to say: "I am a professional person and if I do my best at my job I have no occasion to bother about the law." As in other worldly matters—forewarned is forearmed. The author deals succinctly and authoritatively on all legal matters concerning hospital work. While the implications of the National Service Act are discussed only in respect of the English Act, nearly all the matters dealt with, e.g. Dangerous Drugs Act, Workmen's Compensation Act, Birth and Death Registration, professional

confidence, etc., come under laws common to both countries. This book should be available in every hospital for study and reference.

*Animal Genetics and Medicine.* By HANS GRÜNEBERG. Pp. xii+296, with 33 illustrations. London: Hamish Hamilton. 1947. Price 21s.

This book is warmly and unreservedly commended to the notice of all who, in the field of medical research, are seeking the causation and the manner of development of human defect and derangement. The author gives full accounts of the causes and mechanisms of development of a large number of inherited pathological characters in the mouse, rat, guinea-pig and rabbit and shows that many are similar or identical with clinical entities in man, and that even in the case of such as have no close counterparts in man, a study of the mechanism of development may be expected to yield new ætiological concepts of value to medicine. It can confidently be expected that this book will exert a profound influence on medical research in the immediate future.

*The Rotunda Hospital, 1745-1945.* By O'DONNELL T. D. BROWNE, M.B., M.A., M.A.O. (UNIV. DUBL.), F.R.C.P.(I.), F.R.C.O.G. Pp. xx+296, with 44 illustrations. Edinburgh: E. & S. Livingstone. 1947. Price 42s.

The bicentenary of the Rotunda Hospital was celebrated in Dublin in July of this year by an International Congress of Obstetrics and Gynæcology, but the timely publication of this splendid volume by the King's Professor of Midwifery in Trinity College will serve as a more lasting commemoration of the same interesting event and enable a wider public to share in the celebration.

In founding the hospital, Dr Bartholomew Mosse, whose appropriate epitaph was "miseris solamen instituit," was like the architect of St Peter's in that "he builded better than he knew." Indeed, so troubled were the finances and the fortunes of the institution in his all-too-short lifetime that he probably had no chance to glimpse its historic future. As "Master" he was the first of twenty-eight obstetricians of varying distinction who have determined its professional standing and made it a famous centre of practical training in obstetrics throughout the last two centuries. Of these, Fielding Ould, Clarke, Collins, Macan, Smyly and Tweedy are the names best known outside Dublin.

The tracing of the growth and development of the hospital, and the analysis of the contribution which the successive masters made to its success and fame, have naturally led the author to outline the coincident development of obstetrics in the last two hundred years. For this reason his book will make an appeal to many who have no personal associations with the Rotunda, although there can be no one with any real knowledge of midwifery to whom its name is unfamiliar. The book should therefore find many eager readers all over the world, and it is to be commended not only for the value of its contents but for the easy lucidity of the author's style.

A special word of praise is due to the publishers for the wholly admirable format, which makes the book a worthy memorial.

*Atlas of Bacteriology.* By R. CRANSTON LOW, M.D., F.R.C.P.E., and T. C. DODDS. Pp. vii+105, with 167 coloured illustrations. Edinburgh: E. & S. Livingstone. 1947. Price 32s. 6d. net.

This work is intended primarily to illustrate what the student hears in lectures or reads in a textbook. It is simply a series of pictures without explanatory text. In dealing with each organism a definite plan has been followed. First the organism is shown microscopically in relation to the specimen obtained clinically, then in a film obtained after culture, and in appropriate cases there are tissue sections or naked-eye views of cultures. Many of the illustrations have been obtained by colour photography, but where this is not suitable careful paintings have been employed. The results are admirable and the technical reproduction is excellent.

This atlas should serve a very useful purpose.

## NEW EDITIONS

*Recent Advances in Medicine.* By G. E. BEAUMONT, M.A., D.M., F.R.C.P., D.P.H., and E. C. DODDS, M.V.O., D.Sc., PH.D., M.D., F.R.C.P., F.R.S. Twelfth Edition. Pp. xii+422, with 42 figures. London: J. & A. Churchill Ltd. 1947. Price 21s.

The last edition of this book was published in 1943 though reprinted in 1944 and 1945; it is not surprising therefore that considerable change has been necessary to bring it up to date. The present issue contains about 100 pages of new material and this has been accomplished by omitting a certain amount of the older text. Introductions of note include a chapter on the antibiotics, and new information is available on the sulphonamides and the vitamins. Primary atypical pneumonia, infective hepatitis, homologous serum jaundice, bone marrow transfusion, thiouracil and thiocyanate therapy are also discussed. The present edition will continue and enhance the popularity and usefulness of this excellent handbook.

*Text-book of Medicine.* By American Authors. Edited by R. L. CECIL, A.B., M.D., SC.D. Seventh Edition. Pp. xxxiii+1730, with 244 illustrations. London: W. B. Saunders Company. 1947. Price 50s. net.

This remarkable text-book which represents the work of more than 150 leading physicians has been extensively revised, and contains a considerable amount of fresh material. Each article, being the work of one who has specially interested himself in the subject, is authoritative and reliable. The text covers the full range of medicine and the sound judgment of the editors has produced a well-balanced whole. The book can be thoroughly recommended and is excellent value at the price.

*Treatment of the Patient Past Fifty.* By E. P. BOAS, M.D. Third Edition. Pp. 479. Chicago: Year Book Publishers. 1947. Price \$5.75.

It is well known that the average age of the population is increasing and that many more are now surviving to later years. As a consequence, care of the aged and ageing forms an ever-increasing feature of the doctor's work. The author devotes several chapters to the ageing process and general questions which arise in the aged. He then describes systematically those diseases which are more common in later life. The book is beautifully produced and is full of helpful information and is one that is well worthy of the attention of every practising doctor.

*Massage and Remedial Exercises in Medical and Surgical Conditions.* By NÖEL M. TIDY, Member of the C.S.M.M.G.; T.M.M.G. Seventh Edition. Pp. 480, with 190 illustrations. Bristol: John Wright & Sons Ltd. 1947. Price 25s.

What practitioner has not at some time or other wished for a greater knowledge of massage and remedial exercises? Many a patient could have his convalescence expedited by the use of appropriate physiotherapy which might be initiated or demonstrated by the doctor. When a masseuse is called in it is desirable that the doctor should know about this branch of therapeutics and discuss it with her. Although this volume has been written mainly for students and practitioners of massage it will be found useful by those medical men who want to revise their knowledge of the subject.

*An Introduction to Dermatology.* By NORMAN WALKER, KT., M.D., LL.D., F.R.C.P., and G. H. PERCIVAL, M.D., PH.D., F.R.C.P.E., D.P.H. Eleventh Edition by G. H. PERCIVAL. Pp. 349, with 233 illustrations, 146 in full colour. Edinburgh: E. & S. Livingstone Ltd. 1947. Price 35s. net.

The eleventh edition of this book has been rewritten and in it the important advances which have been made in medicine since its predecessor in 1939 have been incorporated. It contains a large number of clinical photographs, many of them in

colour, which have been beautifully reproduced. One could perhaps have wished for a greater elaboration of those points at which dermatology and internal medicine meet. This book was never intended to be a complete system, however, and it continues to fulfil the purpose for which it was originally written—to provide a most useful synopsis of the subject for both student and practitioner.

*The Sanitary Inspector's Handbook.* By HENRY H. CLAY. Sixth Edition. Pp. xxii+545, with 99 illustrations. London: H. K. Lewis & Co. Ltd. 1947. Price 22s. net.

As the sub-title states, this is a manual for sanitary inspectors and other public health officers. The field covered is a wide one, including information as to the training, qualifications and duties of sanitary inspectors, and public health law applicable to these duties; housing and building; water supplies, drainage and refuse disposal; food control and control of infectious diseases, and other subjects.

The amount of technical knowledge required of a modern sanitary inspector is very considerable, and this book, already in its sixth edition since it first appeared in 1933, can be thoroughly recommended.

A feature is its excellent illustrations.

*Penicillin in General Practice.* By J. L. HAMILTON-PATERSON, M.D. Second Edition. Pp. 110. New York, Toronto: Staples Press Ltd., London. 1947. Price 5s. net.

Penicillin therapy is still in its infancy and continuous changes in methods and dosage are being reported in the literature. The second edition of this book has been prepared to include these changes and brings the subject up to date.

## BOOKS RECEIVED

- ALLISON, D. RHODES, M.D., M.R.C.P., and GORDON, R. G., M.D., D.S.C., F.R.C.P.  
*Psychotherapy: Its Uses and Limitations.* (Oxford University Press, London) 8s. 6d. net.
- BALLENGER, WILLIAM LINCOLN, M.D., F.A.C.S., and BALLENGER, HOWARD CHARLES, M.D., F.A.C.S., Assisted by BALLENGER, JOHN JACOB, B.S., M.D.  
*Diseases of the Nose, Throat and Ear.* Ninth Edition. (Henry Kimpton, London) 63s. net.
- BROWN, ADOLPH M., M.A., M.D. *Modern Plastic Surgical Prosthetics.* (William Heinemann (Medical Books) Ltd.) 35s. net.
- BURN, J. HAROLD, M.D., F.R.S. *The Background of Therapeutics.* (Oxford University Press, London) 22s. 6d. net.
- BUXTON, O. V., S.R.N., and MACULLOCH MACKAY, P. M., S.R.M.N. *The Nursing of Tuberculosis.* (John Wright & Sons Ltd., Bristol) 7s. 6d.
- EVE, DUNCAN, Jr., M.D., F.A.C.S. *Handbook on Fractures.* (Henry Kimpton, London) 25s. net.
- FISHBEIN, MORRIS, M.D. *A History of The American Medical Association, 1847 to 1947.* (W. B. Saunders Company, London) 50s.
- GARDNER, ERNEST, M.D. *Fundamentals of Neurology.* (W. B. Saunders Company, London) 24s.
- HILL, A. BRADFORD, D.S.C., PH.D. *Principles of Medical Statistics.* Fourth Edition. (The Lancet Limited) 10s. 6d. net.
- KENDALL, JAMES I., PH.D., D.S.C. *Microscopic Anatomy of Vertebrates.* Third Edition. (Henry Kimpton, London) 30s. net.
- RYLE, JOHN A., M.A., M.D., F.R.C.P. *The Natural History of Disease.* Second Edition. (Oxford University Press, London) 22s. 6d. net.
- SCHINDLER, RUDOLF, M.D., F.A.C.P. *Gastritis.* (William Heinemann (Medical Books) Ltd.) 50s. net.
- SCOBEE, RICHARD G., B.A., M.D. *The Oculorotary Muscles.* (Henry Kimpton, London) 40s. net.
- TANGNEY, MARY E., R.N. *Diabetes and The Diabetic in the Community.* (W. B. Saunders Company, London) 14s.

# Edinburgh Medical Journal

March 1948

## A SHORT HISTORY OF THE PNEUMOCOCCUS WITH SPECIAL REFERENCE TO LOBAR PNEUMONIA

By J. T. SMEALL, M.C., M.B., Ch.B., D.P.H.

(Late Bacteriology Department, Royal Infirmary, Edinburgh)

THE clinical entity—pneumonia—has been known since the days of Hippocrates and the old Greek physicians, *i.e.* circa 2300 years, but there can be no doubt that its origin goes back to uncharted medical history. On the other hand, the rôle of the pneumococcus as the *causa morbi* was definitely established just over sixty years ago. Prior to this it had been generally held that the condition was due to exposure, unavoidable or imprudent, to climatic conditions associated with a low temperature, but from the clinical behaviour of the disease and the occurrence of epidemics, it was gradually being realised that it might be due to an infectious process. Two strong advocates of an infectious theory were Jürgensen and Flindt, but even Jürgensen, while believing that pneumonia was an infection, said that a chill was a rare occasional cause. Flindt said that in over 90 per cent. of his cases a chill could with certainty be excluded.

Klebs, in 1875, was the first to investigate the bronchial secretion of a case of pneumonia for pathogenic schizomycetes. Many different organisms were found, which he called monadinen. The monad he thought responsible for the pneumonia he termed monas pulmonale. With only white of egg as a culture medium, Klebs can only be regarded as a pioneer in this particular instance. What were subsequently found to be pneumococci were recovered from an extra-pulmonary source, first by Sternberg, and shortly afterwards by Pasteur, the latter's observations being published first. It was in 1880 that Sternberg infected some of his saliva under the skin of a rabbit and found, fortuitously, that a fatal septicæmia ensued, the blood containing great numbers of oval micrococci. Repetitions of this experiment always produced the same result. His paper, published in 1881, was accompanied by a photomicrograph showing capsulated diplococci and short chains.

Pasteur, a few months later, while investigating rabies, produced a similar septicæmia by infecting rabbits subcutaneously with a little buccal mucus from a child just dead from hydrophobia. The organisms in the rabbit blood were mostly in figures of 8 and were surrounded by



an aureole. The infection could be transmitted from rabbit to rabbit always with the production of a septicæmia. He cultured the organisms in veal broth. For the time being Pasteur was nonplussed, not knowing whether he was dealing with a new disease or one that had some connection with hydrophobia. At any rate he thought it would be rash to say that they were absolutely independent. Early in 1881 his results were intimated to the French Academy of Medicine in Paris. It required five or six meetings of the Academy to clear up the position, when it was shown that a similar condition had been produced by normal saliva and also by that from the mouths of three children dead of bronchopneumonia. The organisms causing this septicæmia were later called the organisms of sputum-septicæmia by Fränkel and found by him to be identical with those causing lobar pneumonia.

In the same year (1881) Eberth examined a case of croupous pneumonia associated with a metastatic meningitis. By the use of methyl-violet he demonstrated microscopically the presence of cocci, in twin form, both in the lung and in the brain ventricles. There can be little doubt that these organisms were pneumococci, but in those inchoate days of bacteriology, his observations were not supported either by culture or animal inoculations. Also in 1881 Koch made sections of the lungs and kidneys from a case of pneumonia. The accompanying photograms showed cocci in pairs. Friedländer, in 1882, published the first of his papers, which were to lead to much controversy. His work will be referred to anon.

The following year Talamon produced an important contribution on the "coccus of pneumonia." Examining 25 cases of lobar pneumonia, he found most often a characteristic ellipsoid diplococcus, which he aptly described as lancet-shaped or lanceolate. In his researches he was hampered by having only a fluid medium (Liebig extract of beef broth) at his disposal, so that he rarely got pure cultures. Thus during life he punctured the consolidated lungs in 8 cases of pneumonia, but was able to obtain only one pure culture of the diplococci. Talamon also carried out a number of animal inoculations, chiefly on rabbits. Sixteen out of 20 died, lanceolate cocci being present in the blood of some of these. Culture of the blood from his 25 cases yielded oval cocci in 2 cases. One curiosity about his work was that he did not observe, or at least did not mention, that the organisms were capsulated. From his investigations Talamon concluded that fibrinous lobar pneumonia was an infectious disease produced by a special microbe of characteristic form, *lanccolée au grain d'orge ou de blé*. Limited to fluid culture his researches were valuable, but not complete.

Returning to the papers of Friedländer, his first dealt with 8 *successive* cases of acute genuine pneumonia. As a pathologist, he examined the bronchial effusion and sections of lung and pleura, describing the presence in all of ellipsoid cocci, mostly as diplococci and some chains of diplococci. In his second paper the number of his cases

of pneumonia had risen to more than 50, in only a few of which were the micrococci missing and these were old cases. Unfortunately, Friedländer goes on to cloud the situation by saying that he had obtained a characteristic growth by stab culture of gelatine. He described it as a nail-form growth, the head of the nail being heaped up on the surface of the gelatine. Another confusing statement was that rabbits were completely refractory to his organism.

Friedländer's results were equivocal. His description of the organisms was homomorphic of pneumococci, and the high incidence of positive cases was unquestionably pneumococcal. On the other hand, the strong growth on the surface of the gelatine, together with the refractoriness of rabbits, suggested that he was not dealing with the pneumococcus in this instance, but what was later called the pneumobacillus. It may be noted that Friedländer was the first to obtain a growth from croupous pneumonia by the use of solid medium.

The spotlight now turns on Fränkel, whose name is definitely linked with the pneumococcus. He first promulgated his views at a Berlin Congress in 1884, when the other main speaker was Jürgensen, the advocate of the infectious theory of pneumonia. His researches were carried out on a comparatively few cases of pneumonia, but he made numerous cultural experiments and animal inoculations. The organism he obtained was a capsule bearing diplococcus of lancet or spindle form. At first he was not sure whether the diplococcus was different from that of Friedländer or a modification differing in virulence. With his eye on two of Friedländer's results, viz. the growth on gelatine and the refractoriness of rabbits, he was at first hesitant when he obtained inconstant results with rabbits and when in one case he got a nail-form growth on gelatine in the first generation. His main work appeared in 1886. By that time he was quite satisfied that his organism was quite different from that grown by Friedländer. He reported that his diplococcus did not grow at room temperature, its growth was more delicate and died out readily unless frequently transferred to fresh media, it rapidly lost its virulence and that it was generally lethal to rabbits, and that it was the real cause of lobar pneumonia.

When confronted with Fränkel's results, Friedländer at once said that there might be different kinds of pneumonia caused by different organisms. For a time Fränkel was influenced by this conception, but at length he came round to the idea of the unity of pneumonia, that is to say, that it was due to only one organism, viz. the pneumococcus. In support of the pneumococcus being the cause of lobar pneumonia, he instanced two cases of empyema following pneumonia from which he had obtained the same organisms as from the lung, and also a case of meningitis complicating a pneumonia from which he had isolated the pneumococcus.

Another important part of Fränkel's work was to prove that the

organisms of the so-called sputum-septicæmia were similar to those found in the lungs in pneumonia. To show that they were inconstantly present in the normal mouth, he instanced his own case. One year his saliva produced regularly a septicæmia in a rabbit, whereas the following year it was quite ineffective. Fränkel knew about the Gram stain, but evidently not as a means of differentiation, and in one of his later papers he acknowledged with gratitude that Weigert had drawn his attention to it as a means of distinguishing his organism from that of Friedländer. He then quotes the original article of Gram. It might be instructive to refer to it here.

We find that the stain was primarily introduced for staining the pneumoniekokken, leaving the background of cells and tissue elements unstained, so that the organisms stood out clearly. Later it was used as a general stain for the organisms of other diseases, and still later a counterstain, such as Bismarck Brown, was employed. As Friedländer's colleague, Gram had investigated 21 cases of pneumonia, the organisms in 19 of which had retained the violet stain, while in the other two they had become decolorised. He mentions the very interesting fact that it was from one of these decolorised organisms that Friedländer had made most of his cultures and animal inoculations. This would certainly account for the growth on gelatine obtained by Friedländer and which so disturbed Fränkel.

The conclusion one comes to is that Friedländer had found pneumococci in most of his cases and the Gram-negative organisms (pneumobacilli) in only a few. White gives support to this view, as had Muir and Ritchie in 1907. There seemed to be an *odium medicum* between Fränkel and Friedländer, especially on the part of Fränkel. Friedländer refers to Fränkel's personal attacks and reproaches. It is only right to point out that independently of Fränkel, Sternberg in 1885 had already come to the conclusion that his salivary coccus was also the same as that causing lobar pneumonia, but his proof was not so conclusive.

In 1886 there appeared the equally important paper of Weichselbaum on acute lung inflammations. His work entailed the examination of 94 cases of lobar pneumonia and 35 other types of pneumonia, and extended over a period of more than two years. Influenced by Friedländer having obtained a growth on gelatine, Weichselbaum had used this medium at first, but always unsuccessfully. He afterwards resorted to agar and blood serum with satisfactory results. His organisms were oval and lancet formed, usually in pairs, but sometimes also round and in chains, and he gave them the name *diplococcus pneumoniae*, a name they still retain. They were obtained from the great majority of his cases, and he concluded that they were the main cause of lobar pneumonia. Streptococci were found in a few cases of both lobar and lobular pneumonia, while Friedländer's organisms (*bacillus pneumoniae*) were obtained pure in 4 cases of lobar pneumonia. Staphylococci were the cause of secondary pneumonias

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only. Weichselbaum's results therefore supported Friedländer's contention that pneumonia may be of various forms caused by different organisms.

### SEROLOGY

Immunity problems soon began to engage the attention of research workers. Already, in 1886, Fränkel had made the observation that when a rabbit had recovered from a subcutaneous inoculation of his diplococcus, it became refractory to further infections of the organism. About the same time Foá and Uffreduzzi had had a somewhat similar experience. Foá, along with different colleagues, continued to take a keen interest in the subject. Thus in 1888, with Bonome, rabbits were immunised with the soluble products of the diplococcus, and later with Scabia a high-grade immunity was obtained with a glycerine extract of the pneumococci. Foá and Carbone reported in 1891 that immune serum had a protective influence in infected mice.

In the same year G. and F. Klemperer carried out immunisation experiments on rabbits, using sputa (pre-critical and post-critical) pleural exudate, glycerine extracts of pneumococci and broth cultures. Both subcutaneous and intravenous routes were employed. The post-critical serum from pneumonia cases proved capable of curing pneumococcal infection in rabbits. Having tested immune serum on themselves and found it harmless, they tried its curative properties on 6 cases of pneumonia, with encouraging results. This was the genesis of serum therapy in the treatment of pneumonia.

Emmerich and Fowitzky also immunised rabbits and found that the degree of immunity obtained varied with the method employed. Thus immunity was incomplete if attenuated cultures of pneumococci were introduced subcutaneously, whereas complete immunity was obtained by the intravenous inoculation of a fully virulent culture. Emmerich, in 1894, prophesied that the serum of immunised animals would undoubtedly in future be used as an ideal healing method in human disease.

The *modus operandi* of an immune serum was given various interpretations by the immunologists of that time. Thus the brothers Klemperer explained it on a toxin-antitoxin basis. In this they were doubtless influenced by the lately published important results of Behring and Kitasato on the toxins and antitoxins of the diphtheria and tetanus bacilli. Emmerich thought it depended on a bactericidal substance in the blood, and Mosny a toxicidal. On the other hand, Issaëff found that phagocytosis played the most important rôle in the acquired immunity. This was a significant finding, but, coming from the Metchnikoff laboratory, not a surprising one. Kruse and Pansini, while admitting phagocytosis, thought it of secondary importance. Later Neufeld thought that the diplococci were rendered more susceptible to phagocytosis by the production of bacteriotropins (opsonins).

So far an important property of immune serum had not been mentioned. It was drawn attention to by Metchnikoff in 1891 in a paper on immunity. He found that the serum of guinea-pigs vaccinated against the vibrio metchnikovi clumped the vibrios, and he interpolated "Elle se rencontre aussi pour le microbe de la pneumonie qui forme dans le serum des lapins vaccinés des paquets de streptocoques très longs." This phenomenon of immune serum had already been reported in the case of *B. pyocyaneus* by Charrin and Roger in 1889.

Metchnikoff's observation was confirmed by Mosny (1892), Arkharow (1892), Issacff (1893), and in this country by Washbourn in 1896. In the words of Washbourn: "When protective serum is inoculated, it appears perfectly clear at the end of 24 hours, but at the bottom a sediment is seen. This sediment consists of pneumococci staining well and grouped in masses." Was this congeries of organisms real agglutination? It would appear so, as normal serum showed only a uniform turbidity.

This phenomenon was more fully studied in 1897 by Bezançon and Griffon and definitely called by them agglutination. These workers were obviously inspired by their association with Widal, who had published his sero-diagnostic method for typhoid fever in 1896. Compared with typhoid fever, they found that the serum of pneumonia cases agglutinated only in low titre and also that some pneumococci were agglutinated and not others. They believed that they had been able to differentiate between pneumococcal races by the agglutinating reaction.

Neufeld contributed a paper on pneumococcal agglutination in 1902. He found that normal serum of both man and animal had no agglutinative effect, so that there was no risk of wrong inferences in this respect. Using broth cultures of pneumococci in his experiments, he found that the highest dilution of rabbit immune serum and convalescent serum of pneumonia cases to cause agglutination was 1:50. Wadsworth cast doubt on agglutination technique prior to Neufeld's experiments. Like Neufeld he used a broth culture, but this was centrifugalised and saline added to the precipitate. He claimed more accurate results from this method.

### TYPE DIFFERENTIATION

Prior to the evidence that varieties of pneumococcus could be distinguished by means of agglutination tests, it had been suspected that more than one type existed. An experience of Foá suggested this. He cultivated two organisms, one from a pneumonia, which he called a pneumococcus, and the other from a meningitis, which unfortunately was called a meningococcus. Later he referred to the latter as meningococcus or streptococcus lanceolatus, and it is generally presumed to have also been a pneumococcus. But without presuming too much, the interest lay in the fact that they were found to be serologically different. There was more satisfactory proof later.

Eyre and Washbourn acquired some anti-pneumococcal serum from Pane of Naples and carried out a series of tests on pneumococci obtained from five different sources. They found that the serum protected against four varieties, but not against the fifth.

It is interesting to note that the first type of pneumococcus to be recognised as different from all others was to become known as Type III. There was nothing dramatic about its discovery. Indeed at first no one even called it a pneumococcus, although it was sometimes described as looking like one. It was rather a case of a conjectural approach, being referred to as a pathogenic diplococcus, a pseudo-pneumococcus, streptococcus mucosus, pneumococcus mucosus and finally Type III. The outstanding feature of this organism was its peculiar mucoid growth on culture. The pathogenic diplococcus, resembling a pneumococcus, was obtained in 1897 by Atkinson from an extra-pulmonary source, while Richardson in 1900-1 reported that during the past five years he had obtained pseudo-pneumococci from 4 cases of lobar pneumonia. Although they had difficulty in giving it a name, Howard and Perkins called their organism streptococcus mucosus.

Schottmüller published papers in 1903 and 1905, but he had first obtained what he called streptococcus mucosus from a parametritis in 1896. Since then he had found it in pus at different times and also in the blood in cases of pneumonia.

In 1905, Park and Williams in a study of pneumococci in normal throats and in pneumonic exudates, isolated streptococcus mucosus from 8 cases of pneumonia (twice in pure culture) and also from healthy people. After saying it should be called streptococcus lanceolatus var. mucosus or diplococcus lanceolatus var. mucosus, they themselves rather naïvely said that they gave it the *trivial* name of pneumococcus mucosus. Streptococcus mucosus was also reported from lobar pneumonia cases by Duval and Lewis, and Eng. Fraenkel, and from a case of suppurative otitis by Heim. Neufeld had reported in 1900 that pneumococci were soluble in bile, but none of the observers cited above mentioned that they had made use of this test. The organisms of Park and Williams and Howard and Perkins fermented inulin.

Still calling it streptococcus mucosus, Holman in 1914 isolated it from a case of lobar pneumonia. Hanes, in the same year, obtained it from 9 cases of lobar pneumonia, but called it pneumococcus mucosus. It fermented inulin and was soluble in sodium taurocholate. That there should exist so much confusion between a streptococcus and a pneumococcus is readily understandable, as in this instance the pneumococcus mucosus may be rounder than normal and under certain conditions there is a strong tendency to catenation.

After this hesitant approach to the pneumococcus mucosus, we are indebted to Neufeld and Haendel for further type differentiation. The foundation was laid during their researches in 1912 on pneumococcal healing sera. The most usual pneumococcus reacting with their sera was regarded as typical and named Pneum. I. The next



commonest was called Pneum. Franz—a name derived from that of the immunised horse. Non-reacting types were referred to as atypical.

It was in 1913 that Dochez and Gillespie produced their well-known classification. Using the two strains of pneumococcus most commonly causing pneumonia, they immunised rabbits, and with the sera obtained carried out protection and agglutination tests on sixty-two strains of pneumococci. The pneumococci were divided into four groups—I, II, III and IV.

I and II groups reacted with the antisera obtained from the rabbits.

Group III, or mucosus group, had distinctive growth characteristics.

Group IV a heterogeneous group.

Cole in 1915 called the four groups types, but he preferred to call Type IV Group IV. Neufeld's types were obtained from Germany and compared with the American types. His Pneum. I corresponded with their Type I, and Pneum. Franz was identified as their Type II. Dochez and Avery in 1917 made an important discovery when they found in young pneumococcal cultures a substance specifically reacting with the homologous immune serum. This suggested to them that if present *in vitro*, it would also be found in the animal body; and it was so. It was demonstrable in the blood and urine of inoculated rabbits and also in the blood and urine of a percentage of cases of lobar pneumonia in human beings. The amount present in the urine was held to be a measure of the severity of the infection and was therefore of prognostic value. The type of the infecting pneumococcus could be determined by a precipitin test. Neufeld had already shown in 1900 that pneumococci dissolved in bile yielded a precipitate when tested with homologous antiserum.

The specific soluble substance (S.S.S.) was found to be derived from the carbohydrate in the capsule. Chemically it was a complex polysaccharide, quite distinct in Types I, II, and III. The nucleoprotein in the body of the coccus was common to all pneumococci, irrespective of type. It is paradoxical that the kernel of type specificity is inherent in the capsule.

Heidelberger along with Avery and other associates investigated the chemistry and immunology of the capsular polysaccharides. As originally isolated these carbohydrates were found to be non-antigenic. In 1925 Avery and Neill found that intact pneumococci acted as complete antigens, while pneumococci in solution, although retaining their type specificity, did not stimulate the formation of antibodies. On this point Avery and Heidelberger concluded that the carbohydrate in the intact cell was combined with some substance which empowered it to act as an antigen, but when this combination was broken up on dissolution of the cell, the carbohydrate could no longer act as an antigen.

A certain combination was reported by Avery and Goebel in 1933, who showed that an acetyl group was attached to the polysaccharide

of Type I pneumococcus. If the acetyl groups were removed during extraction and purification the deacetylated polysaccharide lost its antigenic properties. A contrary opinion was put forward by Felton and Prescott in 1939. In a comparative study of the Type I polysaccharide isolated by the calcium phosphate method and the method of Heidelberger, they concluded that the presence or absence of the acetyl group was of no significance for its antigenicity in white mice. Zozaya and Clark found that the polysaccharides of Types I, II and III did not lose their antigenic properties in mice if they were adsorbed on collodion particles and carbon.

While pneumococci were being investigated from the chemical side the original American classification was not allowed to remain static. At first Types I, II and III were regarded as fixed types, but only Type I has remained immutable. In 1915 Avery found that with certain strains the agglutination reaction with Type II antiserum was sometimes incomplete and less prompt. Using univalent immune sera against ten such strains, he divided them into three subgroups of Type II, viz. Subgroup II<sub>A</sub>, Subgroup II<sub>B</sub> and Subgroup II<sub>X</sub>. Subgroup II<sub>A</sub> and Subgroup II<sub>B</sub> were later identified as Type V and Type VI respectively, while from Type III, Type VIII was hived off after Sugg *et al.* had reported atypical Type III.

The next obvious step was the disintegration of the heterogeneous Group IV. Many tentative attempts were made towards this end. Thus, in 1916-17, Olmstead investigated 94 Group IV strains and demonstrated twelve distinct groups, leaving some of the strains undifferentiated. Griffith, from forty-nine strains, distinguished twelve types including Type II, Subgroups A and B, and Robinson, in 1927, from sixty-five strains obtained eight immunological groups, but nothing of a permanent value resulted from their efforts.

It was not till 1929 that Cooper and her associates placed the segregation of Group IV organisms on a sound basis. Using monovalent antisera, 120 strains from lobar pneumonia cases were divided into ten groups, IV to XIII, leaving some unclassified. In 1932 they extended their types from XIV to XXXII. At the same time some of the types obtained by Avery, Griffith, and Robinson were correlated. Kaufmann *et al.* in 1940 reported twenty new types, sixteen of them being subtypes. These included some already described by Vamman. A new type was determined not only by capsular swelling, but by agglutination and absorption tests. The new types were all serologically distinct from those of Cooper, but as some were antigenically related, Cooper's numbers were retained and a letter added. They said that fifty types were now known, but that presumably the number of types was far beyond a hundred.

In 1941 Walter *et al.* classified a thousand cultures in seventeen new types, some of which corresponded to those of Kaufmann. They comprised nine new types and eight subtypes. Cooper's Types XXVI and XXX were replaced by new types. There were now forty types

and fifteen subtypes. Morch (1942) said that the studies commenced by Kaufmann *et al.* had been continued and eighteen new types established. Eddy (1944), in order to avoid confusion, recommended that every type should be given a different number regardless of its antigenic relationship to other types. Seventy-five types were listed. It should be mentioned that, *pari passu* with the American classification, Lister in South Africa had commenced a system of grouping, which promised to be of equal importance, but it became subordinated to the American system. Ordman has correlated the types found in South Africa and in the U.S.A.

#### ADDENDA

It is true, as Don Quixote has said, that in the nests of the last year there are no birds of this year. It is also true to say that the past contains the germs of the future, and it is from this viewpoint that the subject of this paper has been approached.

The history of this interesting organism in modern times is, or should be, well enough known, whereas knowledge of its early beginnings is not so easy of access. Since its first recognition sixty-odd years ago, the pneumococcus has been christened a score of times. The list may be found in *The Biology of Pneumococcus* by White. The specific name is *diplococcus pneumoniae* (first given to it by Weichselbaum), but the familiar name pneumococcus, that is to say lung coccus, although it takes no cognisance of its activities outside the lung, will almost certainly continue to be popular. The term pneumokokkus was used by Klein in 1884, while Fränkel employed it only sparingly, his usual nomenclature being pneumoniecoccus or pneumoniemikrococcus.

A chill, once held to be of prime importance in the causation of pneumonia, is now considered as only a possible contributory factor, just as any other debilitating influence, such as fatigue, alcoholism, injury, and so on. Old ideas, however, die hard, and many people still have an affecting belief in a chill as the *fons et origo* not only of pneumonia but many of their other illnesses. Thus if a doctor diagnoses a chill it serves a dual purpose, not only satisfying the patient, but at the same time affording the medical man a ready escape from all etiological difficulties.

It was at one time suggested that pneumonia might be of pythogenic origin. This meant it could be caused by inspiring emanations from foul matter, for example defective drains. It may be recalled that this was once thought to be the origin of typhoid fever. This theory has long since been forgotten. Yet is it not strange that the medical profession perpetuates a similar mistaken diagnosis in the name of a very important disease, namely malaria, a name that to those who are at all word conscious still conjures up visions of reeking swamps! Still another theory may be referred to only to be dismissed. A telluric origin was suggested by Prof. Purjesz, who rejected both the

infectious and a *frigor* theories and thought that pneumonia was due to some underground disturbance. This idea soon went *zu grunde*, as the Germans say, and appropriately so in this case.

The infectious theory did not meet with general acceptance for some time. Indecision is reflected in an article in the *Lancet* of 2nd April 1892, and remember this was six years after the apparently conclusive findings of Fränkel and Weichselbaum. There we find the following views: "The pathology of pneumonia is one of the *questiones vexatæ* of Medicine"; "Much remains to be done before we are in a position to conclude that bacteriology has said the last word regarding pneumonia"; and finally, "It will thus be seen that the pathology of pneumonia remains a question *sub judice*, but that the best authorities more and more incline to the specific theory of its origin."

The fact that pneumococci were not uncommon denizens of the normal oro-pharynx stuck in the throats of many. It puzzled them how such apparently harmless organisms could cause pneumonia. They did not know at that time that there were many types of pneumococci, varying greatly in virulence, and that these oral types caused only about 25 per cent. of cases of pneumonia, the disease in the main being due to infection from without. In 1900 Bezançon and Griffon during their agglutination experiments concluded, rather erroneously, that pneumonia in the majority of cases was due to these indwelling pneumococci.

Attention should be drawn here to a remarkable instance of prescience. Sternberg in 1885, after admitting that autoinfection may occur, went on to say: "A person whose vital resisting power is reduced by any of the causes mentioned may be attacked by pneumonia from external infection with material containing a pathogenic variety of this micrococcus having a potency, permanent or acquired, greater than that possessed by the same organism in normal buccal secretions." This is a prediction worthy of Nostradamus.

The serum therapy for the treatment of pneumonia, foreshadowed by the Klemperers and Emmerich, could not be put on a rational basis until the type of the infecting organism could be determined and thus had to wait over twenty years. At first it was used only for Type I and Type II pneumonias, a Type III antiserum being difficult to obtain. As time went on and the type of some of the Group IV organisms was determined, sera for the more usual types causing pneumonia were made and used especially in the U.S.A. They were not available for general use in this country. Serum treatment, if available, was the recognised rational therapy till the advent of the sulphonamide drugs in 1938, the first being sulphapyridine. This new treatment involved no type differentiation and thus could be applied equally well to any case of pneumonia. In their time they have been more or less superseded by penicillin, but they are still of use in penicillin resistant cases.

The usual method of determining the type of the infecting pneumococcus was by the intraperitoneal inoculation of a mouse with a

specimen of sputum and subsequent application of the agglutination test to the peritoneal exudate. The agglutination test gave way to Neufeld's quellung reaction, which had lain fallow for over two decades, and which was applicable either to the direct examination of the sputum or to the peritoneal exudate of the mouse.

The sluice-gates of literature have, in truth, been opened on the pneumococcus, and references have perforce had to be selective and in the hope that there has been no flagrant omission. This paper does not presume to be other than a parergon.

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# SUPERFICIAL PHLEBITIS

## Ambulatory Treatment With Elastoplast Bandaging

**Case History.** L.L. Aged 42. A female Sugar Packer. Whilst at work on June 16th, 1946, she cut the outer side of her left ankle: shortly afterwards a septic eczema of the ankle area supervened. On July 26th a large clot appeared in the internal saphenous vein on the inner side of the calf (Fig. 1).

**Treatment.** August 9th, 1946. A well-bevelled adhesive sponge rubber pad was placed over the clot, the eczema was covered by layers of Viscopaste and the leg firmly bandaged with Elastoplast from toes to knee (Fig. 2). August 23rd, 1946. There was no pain or soreness in contrast to the presence of both before treatment. Eczema was cleaned with calamine in oil, and dressed with Jelonet and Ichthopaste. The pressure pad was re-applied and the leg again firmly bandaged with Elastoplast.

August 30th, 1946. Treatment repeated. September 27th, 1946. Clot completely disappeared, leg comfortable, eczema largely cleared up and internal saphenous vein sclerosed and obliterated (Fig. 3).

**Comment.** An example of ambulatory treatment of Phlebitis by local pressure over clot and firm bandaging, resulting in its speedy obliteration and in the restoration of the leg to normal condition. Details and illustrations above are of an actual case. T. J. Smith & Nephew, Ltd., Manufacturers of Elastoplast, Viscopaste, Jelonet and Ichthopaste are privileged to publish this instance, typical of many, in which their products have been used with success, in the belief that such authentic records will be of general interest.



Fig. 1 above Fig. 2 below



Fig.

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# THE PREPARATION OF ISO-OSMOTIC PHOSPHATE BUFFER SOLUTIONS

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THE problems encountered in this paper arose during some work on the osmotic behaviour of erythrocytes, and the results are published in the belief that they may be of value in other branches of biological research. Phosphate buffer systems are in such wide use in biochemistry that their importance need not be emphasised. As ordinarily used, they consist of varying mixtures of M/15  $\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$  and M/15  $\text{KH}_2\text{PO}_4$ , and while such mixtures control pH admirably, they have certain inherent defects. In particular, although the parent solutions have the same molarity, they, and the buffer mixtures derived from them, have different osmotic pressures. The problem with which the writer was confronted was the preparation of phosphate buffer solutions of varying pH, but of constant osmotic pressure.

The reasons for a combination of sodium and potassium salts when the use of a common cation would eliminate one variable seem to be lost in antiquity. The only explanation that can be traced lies in the fact that  $\text{KH}_2\text{PO}_4$  has the virtue of crystallising in the anhydrous state, and unless hydrates are perfectly stable water of crystallisation has a considerable nuisance value.

Good crystalline A.R. specimens of  $\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$  and of  $\text{NaH}_2\text{PO}_4 \cdot 2\text{H}_2\text{O}$  were analysed for their water content under three different sets of conditions. The results are shown in Table I.

TABLE I

Theoretical Water of Crystallisation.	60.37 per cent.	23.08 per cent.
Methods of Drying.	$\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$ .	$\text{NaH}_2\text{PO}_4 \cdot 2\text{H}_2\text{O}$ .
Over $\text{P}_2\text{O}_5$ : <i>in vacuo</i> : at 18° C. . . .	54.70 per cent.	23.17 per cent.
Over $\text{H}_2\text{SO}_4$ : <i>in vacuo</i> : at 100° C. . .	57.84    "	23.04    "
Electric oven: 120-130° C. . . . .	58.22    "	23.16    "

The hydrate  $\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$  is obviously quite unsuitable for the preparation of standard solutions; but the hydrate  $\text{NaH}_2\text{PO}_4 \cdot 2\text{H}_2\text{O}$  appears to be quite reliable. It may be mentioned at this point that there is no danger of loss of water of constitution at the temperatures employed. Both salts, on heating, give rise to pyrophosphates; the monosodium orthophosphate begins to decompose at 190° C., the disodium orthophosphate at 230° C.

According to Clark (1928) the preparation of the stable hydrate  $\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$  (sometimes known as "Sørensen's Salt") consists of "... exposing to the ordinary atmosphere the crystals containing twelve moles of water. An exposure of two weeks is generally sufficient." Apart from the possibility of absorption of carbon dioxide and other acidic vapours, the writer has been quite unable to confirm this statement. The specimen of  $\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$  referred to in Table I was exposed to atmospheric air for 14 days and was found still to contain 53.8 per cent. of water which could be removed by  $\text{H}_2\text{SO}_4$  *in vacuo*, at  $100^\circ\text{C}$ . (Theoretical for  $\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$ :  $\text{H}_2\text{O} = 20.20$  per cent.)

These considerations and results led to the decision to prepare the phosphate buffers from sodium salts only, and in order to avoid all possible confusion anhydrous samples of the two salts were prepared by heating the hydrates to constant weight at temperatures not exceeding  $125^\circ\text{C}$ . The anhydrous salts were stored in a desiccator over  $\text{H}_2\text{SO}_4$  and in presence of some soda lime. Further drying of these anhydrous specimens over  $\text{H}_2\text{SO}_4$  *in vacuo* at  $100^\circ\text{C}$ . showed that they had moisture contents of  $\text{Na}_2\text{HPO}_4 = 0.01$  per cent.  $\text{NaH}_2\text{PO}_4 = 0.04$  per cent. In the following work all weights are expressed in terms of the *anhydrous* salts only.

It has already been mentioned that equimolecular solutions of these two salts are not iso-osmotic, and the preparation of iso-osmotic solutions is by no means simple. The published literature gives no help on the subject.

In the first place,  $\text{NaH}_2\text{PO}_4$  is to be regarded essentially as a binary electrolyte, while  $\text{Na}_2\text{HPO}_4$  is essentially a ternary one. In the second place, the  $\text{H}_2\text{PO}_4^-$  ion (derived from  $\text{NaH}_2\text{PO}_4$ ) can, and does, ionise further to a slight extent; an M/15 solution of this salt has a  $\text{pH}$  of approximately 4.5. In the third place, the disodium salt undergoes a certain amount of salt hydrolysis; in M/15 solution it has a  $\text{pH}$  of approximately 9.1. And finally, there is the possibility of the production of  $\text{PO}_4^{=}$  ions from either of the salts.

In such a buffer mixture there are, at least theoretically, all of the following osmotically active particles:  $\text{NaH}_2\text{PO}_4$ ;  $\text{Na}_2\text{HPO}_4$ ;  $\text{Na}^+$ ;  $\text{H}^+$ ;  $\text{H}_2\text{PO}_4^-$ ;  $\text{HPO}_4^-$ ;  $\text{OH}^-$ ; and  $\text{PO}_4^{=}$ .

Complex as the system appears to be, it is nevertheless susceptible of investigation. There is no reliable, direct method of determining the osmotic pressure of an electrolyte; recourse must be made to indirect methods involving the depression of the freezing-point or the electrical conductivity. The writer does not propose to become involved in a discussion of the modifications which have been introduced into the original Arrhenius Theory of Ionisation. It will be sufficient to say that the osmotic pressure of a solution of a strong electrolyte can be calculated from the "apparent" degree of ionisation, although modern theory holds that ionisation of a strong electrolyte is always complete, and that experimental deviations from the theoretical values

are due to the fact that ionic mobilities depend upon concentration, and that in any solution of finite (as opposed to infinite) dilution, interionic forces prevent the complete freedom of movement of the ions. The determination of the "apparent" degree of ionisation, whatever its true interpretation, is essential for calculation of the osmotic pressure, and the expression is therefore used in its original sense.

The obvious method of choice is that of the depression of the freezing-point which measures the sum-total of the osmotically active particles. Unfortunately, solutions of  $\text{NaH}_2\text{PO}_4$  and of  $\text{Na}_2\text{HPO}_4$  (especially the latter) undergo considerable supercooling, which introduces an appreciable error by causing an abnormally large amount of ice to crystallise out and so altering the concentration of the liquid phase. The great tedium involved tends to make the procedure a test of stamina rather than of technical skill. Artificial induction of freezing by the addition of a crystal of ice is not to be recommended in the most accurate work. The results by this method tend to be irregular, and they lack a high degree of reproducibility, nevertheless, the averaging of a sufficient number of determinations gives figures which are reliable to within about 1 per cent. Conductivity determinations are more satisfactory, but require more elaborate apparatus and greater technical precautions. Both methods have been used.

#### CONDUCTIVITY METHOD

A Conductivity Bridge operated from a 1000 cycles/second Cambridge Reed Hummer was used. The conductivity cell was of the Kohlrausch pattern and was found to have a cell constant of 0.1980 when standardised with the usual potassium chloride solutions. All measurements were made in a water thermostat controlled at  $25.00 \pm 0.02^\circ \text{C}$ . The water employed for making up the solutions had been redistilled over permanganate in an all-glass Pyrex distillation apparatus protected from the atmosphere. It had a specific conductivity of  $1.68 \times 10^{-6}$  r.o. For the purposes of determining the equivalent conductivity, the equivalent weights of the two salts are taken as  $1/3 \text{ NaH}_2\text{PO}_4 (= 40.03)$  and  $1/3 \text{ Na}_2\text{HPO}_4 (= 47.33)$ .

##### (A) *Solutions of Sodium Dihydrogen Phosphate*

The following results were obtained :—

TABLE II

Concentration. gm. $\text{NaH}_2\text{PO}_4$ /100 c.c.	Resistance (ohms).	Equivalent Conductivity (A).
1.100	33.2	21.7
1.000	36.0	22.0
0.900	39.8	22.2
0.800	44.5	22.3
0.700	49.9	22.6
0.600	57.4	23.0
0.500	68.4	23.1
0.400	84.1	23.6

When the equivalent conductivity is plotted against the square root of the concentration, a straight-line graph is obtained (Graph A in Fig. 1), and when this graph is produced to zero concentration (*i.e.* infinite dilution)  $\Lambda_{\infty}$  is found to be 26.5. This value is assumed, with some justification, to be the equivalent conductivity of the salt at infinite dilution, provided that it continues to ionise as a binary electrolyte. Both in theory and in practice this value is a purely hypothetical one, for at higher dilutions the following figures are obtained :—

TABLE III

Concentration, gm. $\text{NaH}_2\text{PO}_4/100$ c.c.	Volume containing 1 gm.-equiv. (litres).	Resistance (ohms).	Equivalent Conductivity, ( $\Lambda$ ).
0.0800	50	378	26.1
0.0400	100	735	26.8
0.0160	250	1,760	27.6
0.00800	500	3,470	27.7
0.00400	1000	6,640	28.2
0.00160	2500	15,200	28.4
0.000800	5000	26,400	29.1

When the equivalent conductivity is plotted against the square root of the concentrations for dilutions of 50-5000 litres, a second straight-line graph is obtained (Graph B in Fig. 1) and the slopes of the two graphs (A and B) are quite different. At these higher dilutions the further ionisation of the  $\text{H}_2\text{PO}_4^-$  ion is evidently significant. At the highest of these dilutions ( $v = 5000$ ) there is a suggestion that the last stage of ionisation is beginning to occur.

(B) *Solutions of Disodium Hydrogen Phosphate*

The following results were obtained :—

TABLE IV

Concentration, gm. $\text{Na}_2\text{HPO}_4/100$ c.c.	Resistance (ohms).	Equivalent Conductivity, ( $\Lambda$ ).
0.800	24.3	48.3
0.700	27.2	49.2
0.600	30.8	50.6
0.500	35.9	52.3
0.400	43.9	53.3
0.300	56.8	54.9
0.200	82.6	56.5

When the equivalent conductivity is plotted against the square root of the concentration, a straight-line graph is obtained (Graph A in Fig. 2), and when this graph is produced to zero concentration the value of  $\Lambda_{\infty}$  is found to be 65.0. As before, it is assumed that this figure is the hypothetical value for the equivalent conductivity at infinite

dilution, provided that the salt continued to ionise as a ternary electrolyte. As with the monosodium salt, a different graph is obtained at higher dilutions.

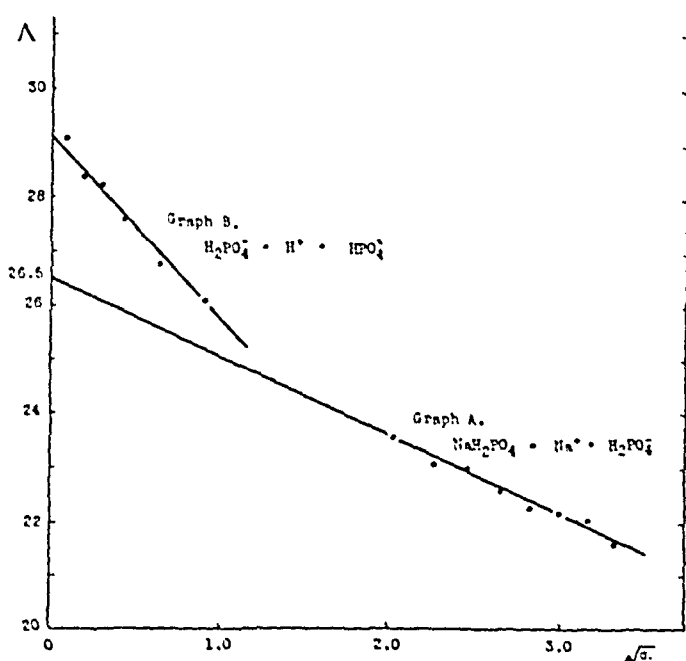


FIG. 1.—Showing the relationship between  $\Lambda$  and  $\sqrt{c}$  (in gm./litre) for solutions of sodium dihydrogen phosphate.

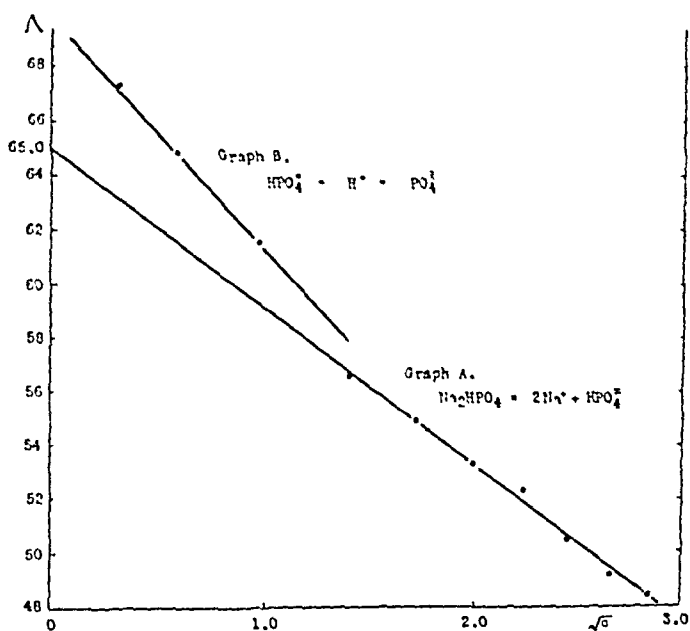


FIG. 2.—Showing the relationship between  $\Lambda$  and  $\sqrt{c}$  (in gm./litre) for solutions of disodium hydrogen phosphate.

When the equivalent conductivity is plotted against the square root of the concentrations for dilutions of 50-500 litres, a second straight-line graph is obtained (Graph B in Fig. 2) and again the slopes of the two graphs A and B are different, indicating that at the higher dilutions

the further ionisation of the  $\text{HPO}_4^-$  ion is significant. At still higher dilutions the equivalent conductivity begins to fall off rapidly due to the absorption of carbon dioxide from the atmosphere, causing a relatively great alteration in conductivity.

TABLE V

Concentration. gm. $\text{Na}_2\text{HPO}_4$ /100 c.c.	Volume containing 1 gm.-equiv. (litres).	Resistance (ohms).	Equivalent Conductivity. ( $\Lambda$ ).
0.0947	50	161	61.5
0.04733	100	306	64.7
0.00947	500	1,455	67.2

(C) *Mixtures of Solutions of  $\text{NaH}_2\text{PO}_4$  and  $\text{Na}_2\text{HPO}_4$*

When the concentrations of these salts are plotted against the measured resistances (from the data given in Tables II and IV) two smooth parabolic curves are obtained. From these graphs can be read off the concentration of each salt required to produce a solution of any selected resistance. For example, the following pairs of solutions should have the same resistance:—

$$\left. \begin{array}{l} 0.732 \text{ gm. } \text{NaH}_2\text{PO}_4/100 \text{ c.c.} \\ 0.361 \text{ gm. } \text{Na}_2\text{HPO}_4/100 \text{ c.c.} \end{array} \right\} \omega = 48.0 \text{ ohms.}$$

$$\left. \begin{array}{l} 0.944 \text{ gm. } \text{NaH}_2\text{PO}_4/100 \text{ c.c.} \\ 0.469 \text{ gm. } \text{Na}_2\text{HPO}_4/100 \text{ c.c.} \end{array} \right\} \omega = 38.0 \text{ ohms.}$$

Table VI records the resistances observed when these pairs of solutions are mixed together in varying proportions.

TABLE VI

$\text{NaH}_2\text{PO}_4$ Solution. 0.732 gm./100 c.c. Volume used (c.c.).	$\text{Na}_2\text{HPO}_4$ Solution. 0.361 gm./100 c.c. Volume used (c.c.).	Resistance found (ohms).	pH (Marconi pH-Meter).
250	0	48.0	4.44
200	50	48.5	5.87
150	100	48.5	6.30
100	150	48.3	6.66
50	200	48.5	7.09
0	250	48.6	8.83
$\text{NaH}_2\text{PO}_4$ Solution. 0.944 gm./100 c.c. Volume used (c.c.).	$\text{Na}_2\text{HPO}_4$ Solution. 0.469 gm./100 c.c. Volume used (c.c.).	Resistance found (ohms).	pH (Marconi pH-Meter).
250	0	38.4	4.41
200	50	38.3	5.86
150	100	38.8	6.30
100	150	38.9	6.65
50	200	38.6	7.09
0	250	38.7	8.85

It appears that when solutions of these two phosphates, each having the same resistance, are mixed together in any proportion the

resistances of the mixtures are the same as those of the parent solutions. When added together solutions of the two salts apparently behave as an ideal mixture, *within the limits of accuracy of conductivity measurements*. That the mixtures are not truly ideal is shown by the variation in  $pH$  which is recorded in Table VI. A solution of  $NaH_2PO_4$  owes its acidity to a certain amount of  $H^+$  derived from the  $H_2PO_4^-$ ; a solution of  $Na_2HPO_4$  is alkaline due to liberation of  $OH^-$  from water as a result of salt hydrolysis; when the two are mixed together partial neutralisation occurs, but the concentrations of ions involved in this chemical reaction is so small that it does not affect the conductivity measurements.

A solution containing 0.732 gm.  $NaH_2PO_4$ /100 c.c. is 0.0610  $M$ . If it is 85 per cent. ionised, the  $[Na^+] = [H_2PO_4^-] = 0.0519 N$ , and the total ion concentration from these sources is 0.1038  $N$ . The  $pH$  of this solution is 4.44 hence the  $[H^+] = 0.0000363 N$  which is approximately 0.035 per cent. of the total ion concentration. Even allowing for the very high mobility of the hydrogen ion, it can contribute very little to the total conductivity. By similar arguments it can be deduced that the  $[OH^-]$  derived from  $Na_2HPO_4$  by salt hydrolysis has also an insignificant effect on the conductivity.

If these two salts behave ideally when their solutions are mixed, it could be argued that, if we add 100 c.c. of  $Na_2HPO_4$  solution to 100 c.c. of  $NaH_2PO_4$  solution (both having the same electrical resistance), then the  $NaH_2PO_4$  solution has been diluted with 100 c.c. of water (containing, incidentally, some  $Na_2HPO_4$ ), and hence the equivalent conductivity should be disproportionately increased since the degree of ionisation increases with increasing dilution; and *vice versa*. But it must be remembered that both have the sodium ion in common, and its presence in the  $Na_2HPO_4$  solution will prevent any appreciable increase in the degree of ionisation of the  $NaH_2PO_4$ . The sodium ion concentration is of the same order in both solutions.

#### FREEZING-POINT DEPRESSION METHOD

Depression of the freezing-point was measured in the usual way by means of a Beckmann thermometer accurate to 0.002° C.

##### (A) Solutions of $NaH_2PO_4$ and of $Na_2HPO_4$

The following results were obtained with pure solutions of these two salts:—

TABLE VII

Concentration of $NaH_2PO_4$ (gm./100 c.c.).	Depression of the Freezing-Point. ( $\Delta t$ ).	Concentration of $Na_2HPO_4$ (gm./100 c.c.).	Depression of the Freezing-point. ( $\Delta t$ ).
0.800	0.225° C.	0.800	0.252° C.
0.700	0.198°	0.700	0.220°
0.600	0.170°	0.600	0.192°
0.500	0.143°	0.500	0.162°
0.400	0.115°	0.400	0.135°

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When the depression of the freezing-point is plotted against the concentration a straight-line graph for both salts is obtained. These two quantities are directly proportional to each other over the range of concentrations used. From these graphs there can be read off the concentrations of the two salts which will give solutions having the same depression of the freezing-point. When such solutions are mixed together the depression of the freezing-point remains unaltered.

The following solutions should, according to the graphs drawn, have the same depression :—

$$\left. \begin{array}{l} 0.514 \text{ gm. NaH}_2\text{PO}_4/100 \text{ c.c.} \\ 0.445 \text{ gm. Na}_2\text{HPO}_4/100 \text{ c.c.} \end{array} \right\} \Delta t = 0.147^\circ \text{ C.}$$

$$\left. \begin{array}{l} 0.598 \text{ gm. NaH}_2\text{PO}_4/100 \text{ c.c.} \\ 0.523 \text{ gm. Na}_2\text{HPO}_4/100 \text{ c.c.} \end{array} \right\} \Delta t = 0.170^\circ \text{ C.}$$

$$\left. \begin{array}{l} 0.654 \text{ gm. NaH}_2\text{PO}_4/100 \text{ c.c.} \\ 0.576 \text{ gm. Na}_2\text{HPO}_4/100 \text{ c.c.} \end{array} \right\} \Delta t = 0.186^\circ \text{ C.}$$

The following table records the depressions of the freezing-points when these pairs of solutions are mixed together :—

TABLE VIII

NaH <sub>2</sub> PO <sub>4</sub> Solution. 0.514 gm./100 c.c. Volume used (c.c.).	Na <sub>2</sub> HPO <sub>4</sub> Solution. 0.445 gm./100 c.c. Volume used (c.c.).	$\Delta t$ (observed).	pH (Marconi pH-Meter).
100	0	0.151° C.	4.50
80	20	0.151°	6.16
50	50	0.152°	6.73
20	80	0.149°	7.34
0	100	0.151°	8.97
NaH <sub>2</sub> PO <sub>4</sub> Solution. 0.598 gm./100 c.c. Volume used (c.c.).	Na <sub>2</sub> HPO <sub>4</sub> Solution. 0.523 gm./100 c.c. Volume used (c.c.).	$\Delta t$ (observed).	pH (Marconi pH-Meter).
100	0	0.173° C.	4.47
75	25	0.170°	6.24
50	50	0.171°	6.70
25	75	0.170°	7.20
0	100	0.171°	9.10
NaH <sub>2</sub> PO <sub>4</sub> Solution. 0.654 gm./100 c.c. Volume used (c.c.).	Na <sub>2</sub> HPO <sub>4</sub> Solution. 0.576 gm./100 c.c. Volume used (c.c.).	$\Delta t$ (observed).	pH (Marconi pH-Meter).
100	0	0.188° C.	4.48
90	10	0.188°	5.78
50	50	0.180°	6.72
10	90	0.188°	7.64
0	100	0.188°	9.13

Freezing-point depression methods lead to the same conclusion as was reached by conductivity measurements; that a mixture of mono-sodium and disodium phosphate solutions behaves as an ideal mixture within the limits of experimental error.

## CALCULATION OF OSMOTIC PRESSURES

According to classical theory, the calculation of the osmotic pressure of an electrolyte requires a knowledge of the degree of ionisation, and for the present purposes it can be calculated from conductivity measurements by the equation  $\alpha = \Lambda/\Lambda_\infty$ ; and from freezing-point measurements by the equation  $\Delta t = K \cdot \frac{w}{M} \cdot (1 + \alpha)$  for a binary electrolyte such as  $\text{NaH}_2\text{PO}_4$ , or by the equation  $\Delta t = K \cdot \frac{w}{M} \cdot (1 + 2\alpha)$  for a ternary electrolyte such as  $\text{Na}_2\text{HPO}_4$ . The following tables give the calculated values for the apparent degree of ionisation.

From these values the osmotic pressure can be calculated from the equation  $\Pi \cdot V = (1 + \alpha) \cdot RT$  for a binary electrolyte, and from the equation  $\Pi \cdot V = (1 + 2\alpha) \cdot RT$  for a ternary electrolyte. The calculated values for the osmotic pressure are also given in the following tables:—

TABLE IX

*Degree of Ionisation and Osmotic Pressure (in Atmospheres at 25° C.)  
for Solutions of Sodium Dihydrogen Phosphate*

Concentration of $\text{NaH}_2\text{PO}_4$ (gm./100 c.c.)	1.100	1.000	0.900	0.800	0.700	0.600	0.500	0.400
$\alpha$ from conductivity . . .	0.82	0.83	0.835	0.84	0.85	0.865	0.87	0.89
$\alpha$ from F.P. depress. . . .	...	...	...	0.82	0.825	0.83	0.845	0.855
$\Pi$ from conductivity . . .	4.08	3.73	3.36	3.00	2.64	2.28	1.91	1.54
$\Pi$ from F.P. depress. . . .	...	...	...	2.97	2.61	2.24	1.88	1.52
Average value of $\Pi$ . . .	...	...	...	2.99	2.63	2.26	1.89	1.53

TABLE X

*Degree of Ionisation and Osmotic Pressure (in Atmospheres at 25° C.)  
for Solutions of Disodium Hydrogen Phosphate*

Concentration of $\text{Na}_2\text{HPO}_4$ (gm./100 c.c.)	0.800	0.700	0.600	0.500	0.400	0.300	0.200
$\alpha$ from conductivity . . .	0.74	0.755	0.78	0.805	0.82	0.845	0.87
$\alpha$ from F.P. depress. . . .	0.705	0.705	0.72	0.74	0.79	...	...
$\Pi$ from conductivity . . .	3.42	3.02	2.65	2.25	1.82	1.39	0.945
$\Pi$ from F.P. depress. . . .	3.32	2.91	2.52	2.14	1.78	...	...
Average value of $\Pi$ . . .	3.37	2.97	2.59	2.20	1.80	...	...

There is a linear relationship between concentration and osmotic pressure over the ranges described for each salt in Tables IX and X. From the graphs obtained when these quantities are plotted against each other (Fig. 3), there can be read off the concentrations of each salt required to give iso-osmotic solutions.

The following figures have been obtained from accurately drawn graphs using the average values given in Tables IX and X.

Buffer solutions may be made up by mixing different volumes of any of these pairs of standard solutions, the  $pH$  range covered lying between 4.5 and 9.0. Such buffers will be iso-osmotic but not iso-molar.

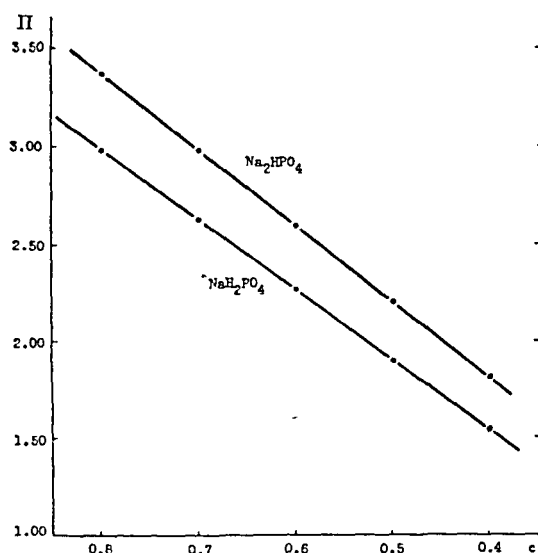


FIG. 3.—Showing the relationship between  $\Pi$  (in atmospheres) and  $c$  (in gm./100 c.c.) for solutions of sodium dihydrogen phosphate and for disodium hydrogen phosphate.

The above range of osmotic pressures (3.00–1.80 atmos.) was chosen because this range covers the span of hæmolysis of normal oxygenated blood. If we assume that "isotonic saline" has

TABLE XI

Osmotic Pressure in Atmospheres at 25° C.	Concentration of NaH <sub>2</sub> PO <sub>4</sub> (gm./100 c.c.).	Concentration of Na <sub>2</sub> HPO <sub>4</sub> (gm./100 c.c.)
3.00	0.802	0.706
2.80	0.748	0.655
2.60	0.694	0.603
2.40	0.639	0.551
2.20	0.584	0.500
2.00	0.530	0.449
1.80	0.475	0.398
6.55	1.80	1.63

$c = 0.85$  gm. NaCl/100 c.c.,  $\alpha = 0.85$ , at  $T = 25^\circ \text{C.}$ , then the calculated osmotic pressure is 6.55 atmospheres. The concentrations of NaH<sub>2</sub>PO<sub>4</sub> and of Na<sub>2</sub>HPO<sub>4</sub> corresponding to this pressure are included in Table XI.

These iso-osmotic buffers should be more useful than the ordinary buffers, especially in experiments involving erythrocytes.

## SUMMARY

1. The use of sodium dihydrogen phosphate in place of the corresponding potassium salt is advocated for the preparation of phosphate buffers.

2. The osmotic pressure of solutions of sodium dihydrogen phosphate and of disodium hydrogen phosphate has been studied by conductivity methods and by depression of the freezing-point. A good measure of agreement between the two methods has been found.

3. Figures are given for the concentrations of each of these salts required to produce iso-osmotic solutions.

4. When iso-osmotic solutions of these two salts are mixed in any proportions the osmotic pressure remains constant, while the  $pH$  varies between the limits of 4.5 and 9.0.

5. It is suggested that iso-osmotic solutions should, for certain purposes, replace the usual iso-molar solutions in the preparation of phosphate buffers.

The author is greatly indebted to Dr T. R. Bolam of the Department of Chemistry, University of Edinburgh, who not only made the Conductivity Apparatus available, but who also discussed these arguments at length with him. He is also indebted to the Earl of Moray Fund of the University for a grant to defray the expenses of this work. Part of this research was carried out while the author held a Crichton Research Fellowship of the University of Edinburgh.

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## MORTALITY FROM APPENDICITIS IN SCOTLAND 1901-45

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OF the 17,701 deaths from appendicitis registered in Scotland between 1901 and 1945, 156 were registered in 1901 and 257 in 1945.

The thought that more men, women, and children could have died in Scotland from appendicitis in 1945 than in 1901 was so disturbing that it drove one to seek for ways in which the stark difference between the 257 deaths in 1945 and the 156 deaths in 1901 might be mollified. On comparing the statistics of these two years in a fourfold table one found a chi squared value of 20.45. This shows that the difference cannot be due to the chances of random sampling; that the increase in deaths cannot be accounted for by an increase in population. The quest, therefore, must be continued through the yearly statistics of population and deaths from appendicitis between 1901 and 1945 (Table A).

But before starting on that quest one must digress upon words and their use, and consider the pictures they call up in the reader's mind. These, and the way in which deaths from appendicitis have been classified in the annual reports of the Registrar General for Scotland, have an important bearing on the present study. To take the last first, appendicitis was not given a separate line in the tables of those reports until 1901 (Registrar General for Scotland, 1904). In 1901 appendicitis was linked with perityphlitis; from 1911-20 with typhlitis; not till 1921 did appendicitis have a line all to itself. Before 1901 appendicitis deaths were included with enteritis deaths. The reasons for this will be seen in the next paragraph.

The part of volume I of the *Oxford English Dictionary*, Anta to Battening, which was ready for publication in November 1885, does not contain the word appendicitis. The reason for this is to be found in the Supplement and Bibliography (1933) which gives:—"Appendicitis (R. H. Fitz, 1886)" and quotes "1886 *Amer. Journ. Med. Sci.*, Oct. 323, as a circumscribed peritonitis is simply one event in the history of inflammation of the appendix, it seems preferable to use the term appendicitis to express the primary condition." Thus, according to Kelly and Hurdon (1905), the word appendicitis appears for the first time, "Quite incidentally and without formal introduction" (op. cit., p. 29). The authors quote a personal letter from R. H. Fitz as stating, "The word was coined by me purely for practical purposes." Kelly and Hurdon describe the confusion of thought about the disease before Fitz coined the word, and show how great was the contribution

of that act of word coining to the advancement of knowledge and clear thought. The authors also tell (*op. cit.*, p. 7), how Mélier in 1827 attempted to clear up the confusion, and how he then prophesied the future possibility of operation. Mélier's attempt at clarification was frustrated by authority.

By coining the word appendicitis Fitz collected the ideas of the pioneers who had been at work during the previous sixty years, and provided a lens which focussed thought and action upon the appendix. An example of this concentration has already been given, for evidently before the word was coined, the Registrar General could not have collected the deaths from the disease under a single heading. The difficulty we have in 1947 in seeing how the disease could have been classified down to 1900 as just one of the many forms of enteritis, illustrates again how thought about the disease has been changed, how action has been focussed upon the appendix since the eighties.

The pictures called up by the word appendicitis range from that in C. P. Scott's cross note (" (i) The Honourable Somebody is nobody, (ii) All those people have appendicitis nowadays, (iii) Sir Frederick Treves operates on all of them ") to those of operations by Professor Caird in the small hours of the morning upon patients who had arrived shortly before in the Royal Infirmary, Edinburgh, in imminent danger of death from appendicitis. Evidently the present study is chiefly concerned with the latter type of case.

From one point of view our language might seem the poorer in having only one word for the wide range of severity illustrated by these two pictures. But that we have only one word is a constant reminder that from the onset of inflammation the patient is in danger until his appendix has been removed, or until the inflammation has obviously subsided. The latter brings, not safety but, the risk of recurrence. That there are also many conditions which are now classified by the Registrar General under the single heading appendicitis is shown by the Manual of the International List of Causes of Death (1940). These conditions are :—

Abscess of the appendix	Pericæcal abscess
Abscess of the iliac fossa	Perityphlitic abscess
Appendicitis (all forms)	Perityphlitis
Appendicular abscess	Post cæcal abscess
Appendicular colic	Rupture of appendix
Inflammation of appendix	Typhlitis.
Inflammation of cæcum	

It is agreed that in each of these the statistics should record the appendix as the origin of the disease. Consideration of the length of the list, the wide range in severity, the rapidity with which its inflammation can cause imminent danger to life, shows how concentration of thought and action upon the appendix benefit the patient's chance of recovery.

The statistics of yearly populations and deaths from appendicitis of men, women, and children of all ages in Scotland, are given in Table A. From these statistics the mean annual death rate over the

DIAGRAM 1

*Annual Death Rates per Hundred Thousand from Appendicitis, All Ages, Both Sexes, Scotland, 1901 to 1945.*

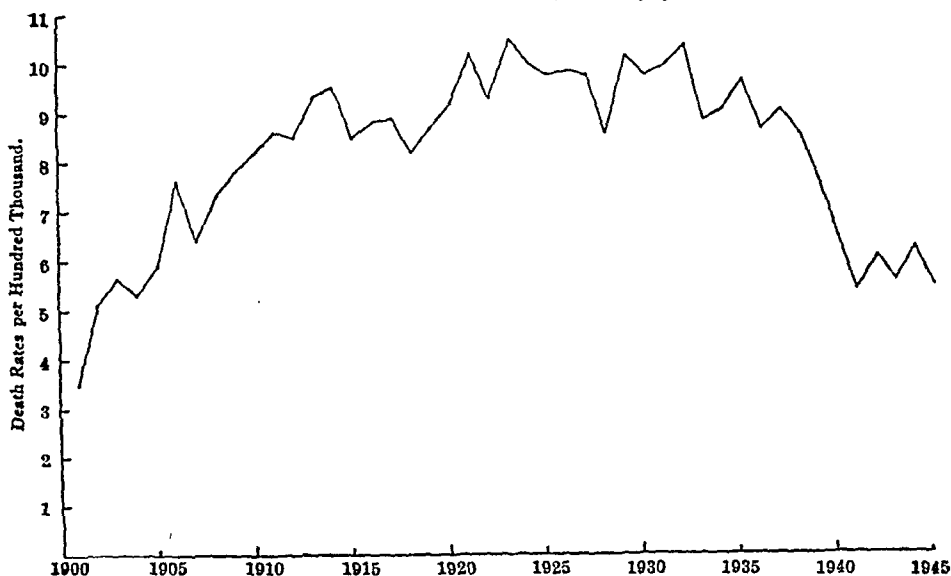


DIAGRAM 2

*Distribution of Yearly Registered Deaths from Appendicitis of People of all Ages in Scotland 1901-45*

1	2	3	4	5	6
Number of Deaths Registered in a Year.	1901-10.	1911-20.	1921-30.	1931-40.	1941-45.
501 and over	.		.	.	
476-500	.		.....	..	
451-475	.	.	.	..	
426-450	.	....		..	
401-425	.	.....	.		
376-400	.			.	
351-375	.	..			
326-350	.	.			
301-325	.	.		.	
276-300	.				..
251-275	.	..			...
226-250	.	..			
Up to 225	.	.			

Mean annual deaths  $394.75 \pm 86.75$ .

whole period is found to be  $8.19 \pm 1.68$  per 100,000, ranging from 3.49 in 1901 to 10.51 in 1923. The yearly rates are illustrated in Diagram 1.



The facts to be grasped in Diagram 1 are the rise in rates from 1901-23, their decline in later years, and their return during the last five years to about the same mortality rates which were recorded during the first decade. In considering Diagram 1 it is well for the reader to remember that these total figures are obtained by adding together the deaths of all ages and each sex, that there are probably differences between the rates for the two sexes and in different age groups, which may be significant and important, and that, even for the total figures, the diagram may give an exaggerated impression of the variation from year to year. That some of these reservations are true and important will be seen later in this study.

Diagram 2 gives the distribution of the actual deaths registered in Scotland between 1901 and 1945.

The noteworthy points are the relatively lower numbers and wide dispersal between 1901 and 1910: the larger numbers and narrower dispersal between 1911 and 1920: the still higher numbers and slightly wider dispersal between 1921 and 1930: the still high numbers, but wider dispersal, overlapping that of 1910-21, in the decade 1931-40: finally the return to the lower numbers of 1901-10, within a narrow range of dispersal, during the five years 1941-45. The same information is conveyed in more measured terms in Table I below:—

TABLE I

*Mean Yearly Registered Deaths from Appendicitis of People of all Ages in Scotland During each of Four Decades and One Period of Five Years*

1	2	3
Period.	Mean Yearly Deaths.	Standard Deviation of Mean.
1901-10 . .	293.9	74.04
1911-20 . .	423.3	18.41
1921-30 . .	479.6	25.25
1931-40 . .	437.7	54.44
1941-45 . .	271.2	18.09
1901-45 . .	394.75	86.75

The dispersal noticed in the Diagram 2 is measured by the standard deviations given in column 3 Table I. The low mean annual figures in column 2 for 1901-10 and 1941-45 again suggest what has been described as a return to the smaller number of annual deaths during 1901-10. But, whereas the mean figure for 1901-10 has the largest standard deviation, the mean for 1940-45 has the smallest standard deviation, approximately equal to that for 1911-20.

Leaving the figures for annual registered deaths and considering the death rates or ratios one reaches the results given in Table II on the following page. Table II illustrates in greater detail the salient facts suggested in Diagram 2. The results in Table II were obtained by applying the method of Brandt and Snedecor, quoted by Fisher (1934) to the statistics for each decade and final five year period, from 1901-45.

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TABLE II  
*Death Ratios, Both Sexes, all Ages, Scotland*

Period.	$\bar{p}$ for Period.	Chi Squared.	P.	Remarks.
1901-10 . .	0.000063	143.63	Less than 0.01	Not homogeneous
1911-20 . .	0.000088	8.93	Between 0.30 and 0.50	Homogeneous
1921-30 . .	0.000098	12.11	Between 0.20 and 0.50	Homogeneous
1931-40 . .	0.000089	61.88	Less than 0.01	Not homogeneous
1931-37 . .	0.000094	12.11	Between 0.05 and 0.10	Homogeneous
1940-45 . .	0.000059	9.28	Between 0.05 and 0.10	Homogeneous

It is evident from Table II that, after the preliminary decade 1901-10, the annual death rates became approximately stable. From 1911-20 the rates range about 9 per 100,000, rising to about 10 per 100,000 during 1921-30. This stability was maintained for only about seven years of the decade 1931-40, round a rate of 9 per 100,000. Between 1937 and 1939 there is a sharp fall in the death rate. From 1940-45 another homogeneous period is formed round a death rate of 6 per 100,000. Thus of the homogeneous periods 1921-30 has the highest period death rate, the next is 1931-37, next 1911-20 and the lowest is the six year period 1940-45.

A glance at column 2, Table II, suggests that the differences between the period death ratios are small enough to be negligible, but this is not supported by testing them as in Table III.

TABLE III  
*Values of Chi Squared for Differences Between Homogeneous Periods*

Periods.	1921-30.	1931-37.	1940-45.
1911-20 . .	26.57	8.208	196.6
1921-30 . .	...	3.371	330.1
1931-37 . .	...	...	247.4

Table III shows that, with the exception of the comparison between 1921-30 and 1931-37, for which the P value of between 0.05 and 0.10 shows the difference to be insignificant, the differences in the five other comparisons between periods are significant. Between 1911 and 1937 the mortality from appendicitis in Scotland, judged by the death rates for both sexes, all ages, showed a slight but significant upward trend. The drop in mortality from appendicitis after 1937 would be more encouraging if it did not correspond with a period when all statistics were being disturbed by the war. In 1939, for example, deaths in H.M. Forces are included in the figures for Scotland, Registrar General (1941) and the population given is that for the usual peacetime 30th June estimate. From 1940 onwards deaths in H.M. Forces are excluded and the populations are mean civilian, based on the National

Register, Registrar General (1946). The Registrar General notes that the withdrawal of selected lives at an age when deaths are normally few would tend slightly to raise the resulting death rate (*op. cit.*, 1946). In 1943 the Mercantile Marine was excluded from the Registrar General's statistics (1945). There was no census in 1941 to correct the estimates of previous years.

One must remember too that the lower rates after 1937 amount roughly to a return to the rates of the first decade which are suspect owing to their lack of homogeneity, suggesting that certifiers had not become accustomed to the new classification. It is true that the fall in death rates reaches stability after 1940, as exemplified by a low mean number of annual deaths, with a low standard deviation, and the homogeneity of the group of ratios 1940-45. But these are not completely satisfactory arguments, so, remembering the various disturbances of statistics due to the war years, one would prefer to suspend judgment on the cause of the fall in death rates after 1937, until strong evidence is forthcoming of a corresponding fall in case mortality. In his note upon the reduction in the number of deaths from appendicitis, Registrar General for Scotland (1946), *op. cit.*, remarks on the figure (258) as "the lowest comparable total on record in Scotland." This remark suggests that he too had doubts about the reliability of the statistics recorded between 1901-10. But, the possibility that the figures in the first decade may give an accurate estimate of the then prevailing annual death rates must not be forgotten.

Comparing the statistics for Scotland and England and Wales after 1935, one finds a similar decrease in mortality between 1937 and 1940: a fall from 7 per 100,000 in 1937 to 6 per 100,000 in 1940, Registrar General (1947) and Monthly Digest of Statistics, no. 19. The stability shown by the statistics for Scotland between 1940 or 1941 and 1945 is not confirmed by the statistics for England and Wales, evidently because, unlike Scotland, there is a further drop in mortality in 1945 in England and Wales. Thus, while the statistics of England and Wales for the years 1941-45 are not homogeneous, those for the years 1941-44 are homogeneous.

In the statistics for England and Wales the mortality rate is 4.46 in 1945 compared with the rate for Scotland of 5.50 per 100,000. If the statistics for Scotland suggest that the decline in mortality has stopped, the statistics for England and Wales suggest the hope of a continuing decrease.

The higher mortality rates in Scotland are exemplified in Table IV on the following page.

Because they give a more reliable distribution of sex and age the statistics of the three census years 1911, 1921, 1931, Table B, have been chosen in this study for the comparison of age and sex differences in appendicitis mortality and for comparison between the mortality in Scotland and in England and Wales (Table IV).

The sex difference in mortality from appendicitis in these three years has been estimated by multiplying the male population in each of ten age groups by the corresponding death rates for females. This gives a series of numbers of "expected deaths." On subtracting the "expected" from the registered deaths the difference is positive in 26 out of the 30 differences given by the statistics for Scotland. The four differences in which the "expected" exceed the registered deaths are found in age group (75 and over) in 1911, and in age groups (5-10), (45-55), (55-65), in 1931. In 1921 all ten differences show an excess of registered over "expected" deaths.

TABLE IV

*Comparison of Death Rates per 100,000, Both Sexes, All Ages, from Appendicitis, in Scotland and in England and Wales*

1	2	3	4	5	6
Years.	Area.	Death Rate per 100,000.	Chi Squared (a).	P.	Significance.
1911	{ Scotland E. and W.	8.61 7.57	} 5.97	Between 0.01 and 0.02	Significant
1921	{ Scotland E. and W.	10.22 7.16	} 54.13	Less than 0.01	Significant
1931	{ Scotland E. and W.	9.95 7.19	} 44.07	Less than 0.01	Significant

(a) Estimated from fourfold tables.

In 1911 the difference in age group (75 and over) is registered 1, "expected" 1.77. In 1931 the differences are, age group (5-10) registered 19, "expected" 24.33; in age group (45-55) registered 28, "expected" 28.26; in age group (55-65) registered 28, "expected" 32.59. As the numbers are small, all these differences appear to be negligible; but it was thought advisable to check the statistics for Scotland with those for England and Wales.

From the statistics for the same years and same age groups in England and Wales a similar series of "expected" deaths was estimated and compared with the series of registered deaths. All 30 differences in England and Wales show an excess of registered over "expected" deaths. This result from the statistics for England and Wales, in which the age group populations are eight to ten times greater than those in Scotland, strengthens the assumption that the 4 differences in Scotland in which "expected" exceed registered deaths are negligible.

Coming next to consider the significance of the differences found. Table V, column 6, gives the results for Scotland in 1931. There it will be seen that the 3 differences in which "expected" exceed registered deaths are insignificant. So also is the one difference in 1911. It may be said therefore that out of the 60 differences in the

two areas, in 56 the registered male deaths exceed the "expected" indicating that in appendicitis the mortality of males is greater than females; and that the 4 differences suggesting the contrary are not greater than can be accounted for by the chances of random sampling.

TABLE V

*Sex Difference in Mortality from Appendicitis, Scotland 1931. Female Death Ratios Applied to Male Populations in Ten Age Groups (Column 3)*

1	2	3	4	5	6
Age Group.	Male Deaths.		$x$	$x^2$	$\frac{x^2}{m}$
	Registered $m+x$ .	Expected $m$ .			
Up to 5	9	6.11	+ 2.89	8.35	1.37
" 10	19	24.33	- 5.33	28.41	1.17
" 15	24	12.19	+11.81	139.48	11.44
" 25	63	38.99	+24.01	576.48	14.79
" 35	26	21.48	+ 4.52	20.43	0.95
" 45	31	21.93	+ 9.07	82.26	3.75
" 55	28	28.26	- 0.26	0.07	0.00
" 65	28	32.59	- 4.59	21.07	0.65
" 75	24	12.96	+11.04	121.88	9.40
75 and over	7	5.01	+ 1.99	3.96	0.79
Diff ...	259	203.85	+65.33	Chi squared = 44.31 ... $n = 9$ $P < 0.01$	
	55.15	...	-10.18		
			+55.15		

TABLE VI

*Sex Difference in Mortality from Appendicitis Male Deaths Registered and "Expected" by Multiplication of Female Death Ratios by Male Populations in Each of Ten Age Groups*

1	2	3	4	5	6
Years.	Area.	Male Deaths.		Difference Cols 3-4.	Chi Squared.
		Registered.	Expected.		
1911	Scotland E. and W.	227 1597	174.68 1063.18	52.32 533.82	36.05 311.68
1921	Scotland E. and W.	282 1474	204.99 1132.73	77.01 341.27	72.85 166.86
1931	Scotland E. and W.	259 1608	203.85 1137.56	55.15 470.44	44.31 250.49

Table VI shows that in each area and each year the total number of registered deaths exceeds the total number of expected deaths. The values of chi squared given in column 6 indicate that each of these

5 differences is significant. Of the 60 differences summarised in Table VI, 35 are significant, 25 are not significant. No age group, however, shows an insignificant difference throughout in both areas. Although in Scotland age group (55-65) shows an insignificant difference in each of the three years, this age group shows significant differences in all three years, in England and Wales. Out of the 6 differences available for each age group, by combining the results from the two areas, 3 or 4 are significant except in age group (75 and over). In this age group 2 differences are significant:—one Scotland 1911, one England and Wales 1931.

It is a fair conclusion that males have a higher mortality from appendicitis than females.

To obtain an indication of the effect of age upon the mortality from appendicitis correlation coefficients were estimated between age group age, age group population, and age group death rates in Scotland and in England and Wales in 1931, the only census year in which five yearly age groups were available throughout life. The results are given below in Table VII.

TABLE VII

*Correlation Coefficients (r) and their Significance, in 1931 for Scotland and for England and Wales*

- (1) Age in 5 year groups.
- (2) Age group populations in 10,000.
- (3) Age group death rates per 100,000.

1	2	3	4	5	6
Area.	Between.	r	t	P	Significance.
Scotland	1 and 2	-0.9696	14.8263	Less than 0.01	Significant
E. and W.	1 and 2	-0.8049	5.0753	" " "	"
Scotland	1 and 3	+0.7725	4.5520	" " "	"
E. and W.	1 and 3	+0.9033	7.8783	" " "	"
Scotland	2 and 3	-0.7290	3.9832	" " "	"
E. and W.	2 and 3	-0.9047	7.9462	" " "	"
Scotland	12.3	-0.9340	18.3721	" " "	"
E. and W.	12.3	+0.0673	0.2433	Greater than 0.80	Becomes insignificant
Scotland	13.2	+0.3920	1.5365	Between 0.10 and 0.20	Becomes insignificant
E. and W.	13.2	+0.6926	3.4631	Less than 0.01	Significance reduced
Scotland	23.1	+0.8264	5.2916	" " "	Sign changed significance increased
E. and W.	23.1	-0.6976	3.5114	" " "	Sign unchanged significance reduced

It will be seen in Table VII that the correlation coefficient between age and death rate ( $r_{13}$ ) is positive and significant; but when the population is held constant ( $r_{13.2}$ ) the significance is lost in Scotland and reduced in England and Wales. This suggests that while in 1931 death rates tended to increase with age the increases depended to some extent on variation in population.



In Table VIII the correlation coefficients for Scotland are compared with those for England and Wales. The coefficients in each area for age and death rates ( $r_{13}$ ) and for population and death rates ( $r_{23}$ ) support one another. The coefficient between age and population ( $r_{12}$ ) for Scotland differs significantly from this coefficient for England and Wales.

TABLE VIII

*Comparison of Correlation Coefficients Given in Table VII for Scotland and for England and Wales*

1	2	3	4	5	6
Area.	Coefficients $r$ Compared.	$z$	Difference $z$ .	Standard Deviation of Difference.	Significance.
Scotland E. and W.	1 and 2 {	$\begin{cases} -2.0850 \\ -1.1122 \end{cases}$	0.9728	$\pm 0.3922$	Significant
E. and W. Scotland	1 and 3 {	$\begin{cases} +1.4898 \\ +1.0265 \end{cases}$	0.4633	$\pm 0.3922$	Not
E. and W. Scotland	2 and 3 {	$\begin{cases} -1.4978 \\ -0.9264 \end{cases}$	0.5714	$\pm 0.3922$	Not

In order to get an estimate of the difference in age group death rates, and their variation in the three census years, the age groups were collected into three arbitrary age periods as in Table IX below.

TABLE IX

*Comparison of Mortality from Appendicitis in Scotland in Three Age Periods in Three Census Years*

1	2	3	4	5	6
Sex.	Age Periods.	1911.	1921.	1931.	Remarks.
Males . .	(a)	10.48	14.89	7.91	1911 and 1931 homogeneous; 1911, 1921, 1931, not homogeneous
Females . .	(a)	8.77	10.36	6.49	1911, 1921, 1931 homogeneous
Both . .	(a)	9.63	12.64	7.20	Not homogeneous
Males . .	(b)	9.60	10.55	11.31	Homogeneous
Females . .	(b)	7.03	7.94	8.44	Homogeneous
Both . .	(b)	8.28	9.18	9.80	Homogeneous
Males . .	(c)	9.01	11.51	16.43	1911 and 1921 homogeneous; 1911, 1921, 1931 not homogeneous
Females . .	(c)	6.15	7.53	13.92	1911 and 1921 homogeneous; 1911, 1921, 1931 not homogeneous
Both . .	(c)	7.41	9.33	15.07	1911 and 1921 homogeneous; 1911, 1921, 1931 not homogeneous

(a) Under 15 years. (b) 15 to 55 years. (c) 55 years and over.

If the figures for 1931, column 5, are taken as an index they will be seen to rise from 7 per 100,000 for both sexes in age period (under 15 years), through 10 per 100,000 in the central age period (15-55), to 15 per 100,000 in age period (55 and over). This confirms the

correlation coefficient ( $r_{13}$ ) in Table VII; but a glance at the figures for both sexes for 1911 (column 3) and 1921 (column 4) shows that in those years this gradation did not occur.

In the variation between the three years there is also gradation. First in the lowest age period the figures for both sexes are not homogeneous. This is seen to be due to the significant rise in male mortality in 1921 (column 6) for the rates for females are homogeneous in the three years. Next in the central age period (15-55) the variation between the years is insignificant for each and both sexes. In the highest age period (55 and over) each and both sexes show an insignificant variation (column 6) between 1911 and 1921 but a significant rise to the highest rates in 1931.

TABLE A

*Number of Deaths from Appendicitis, of People of All Ages, Registered Each Year in Scotland. Corresponding Population*

Years.	Deaths.	Population.	Years.	Deaths.	Population.
1901 . .	156	4,472,103	1924 . .	486	4,881,637
1902 . .	230	4,531,299	1925 . .	479	4,893,032
1903 . .	260	4,579,223	1926 . .	483	4,896,638
1904 . .	243	4,627,656	1927 . .	478	4,891,953
1905 . .	275	4,676,603	1928 . .	423	4,893,182
1906 . .	361	4,726,070	1929 . .	499	4,884,032
1907 . .	308	4,776,063	1930 . .	476	4,845,886
1908 . .	350	4,826,587			
1909 . .	369	4,707,858	1931 . .	482	4,842,980
1910 . .	387	4,737,268	1932 . .	509	4,883,000
1911 . .	410	4,760,904	1933 . .	437	4,912,000
1912 . .	401	4,741,077	1934 . .	451	4,934,000
1913 . .	438	4,728,132	1935 . .	480	4,952,500
1914 . .	453	4,747,167	1936 . .	433	4,966,300
1915 . .	406	4,785,598	1937 . .	452	4,976,600
1916 . .	422	4,824,308	1938 . .	430	4,993,100
1917 . .	430	4,854,738	1939 . .	387	5,006,700
1918 . .	402	4,886,274	1940 . .	316	4,841,200
1919 . .	426	4,894,077			
1920 . .	445	4,864,396	1941 . .	258	4,819,400
1921 . .	499	4,882,497	1942 . .	291	4,751,000
1922 . .	458	4,904,456	1943 . .	259	4,661,600
1923 . .	515	4,901,100	1944 . .	291	4,653,600
			1945 . .	257	4,673,931

Notes: (a) Appendicitis linked with perityphlitis 1901-10 with typhlitis 1911-20.

(b) Populations are census populations in 1911, 1921, 1931. Estimated for 30th June in other years to 1939; in 1940 mean of quarterly estimates of civil population based on National Register, 29th September 1939. Mercantile Marine excluded 1943.

(c) Deaths in H.M. Forces included in 1939; excluded 1940, 1941, 1942, 1943, 1944.

(d) Figures taken from Annual Reports of the Registrar General for Scotland for the years 1901-45.

Table IX demonstrates, what has already been hinted, that a simple answer cannot be given to the simple question "what is the effect of age on the mortality from appendicitis?" The answer to that question can only be relative. Thus by neglecting 1911 and 1921, and taking

1931, the last census year, as an index, the answer given is straightforward; but a census taken in 1941 would probably have given a materially different answer. To expect a simple answer is to assume that the effect of age upon mortality would not change. But the measure of mortality given in Table IX depends on the population in each of the three age periods. Table B shows that the population is not static, on the contrary, while the population in the age period (up to 15) declined the population in the central age period (15-55) remained relatively steady; but in the highest age period (55 and over) the population increased. For example the population of males (75 and over) will be seen in Table B to have increased from about 27,000 in 1911 to 38,000 in 1931. Evidently the effect of age, as measured in this way, will change as the denominator, population, changes through the years.

Keeping these reservations in mind it can be said that in 1931 the death rates per 100,000 were :—(up to 15) 7, (15-55) 10, (55 and over) 15.

If this study has failed to find a satisfactory explanation for the difference between the number of deaths in 1901 and 1945, it does give hope of improvement in mortality after 1937 and for the future. A measure of this improvement is given by considering that, had the 1940 mortality rates prevailed from 1901-45, the number of deaths from appendicitis would have been recorded as 14,100 instead of the 17,701 registered; a saving of 3600 lives. But it is a sad thought that, in spite of the work of the pioneers in France, in the United Kingdom, and in America, since the days of Méliér, and in spite of the publicity given by the illness of Edward VII just before his coronation, a significant decline in the mortality from appendicitis in Scotland only began in 1937.

The study suggests two problems in which research might discover a physical basis for the significant differences in :—

- (i) Male and female mortality.
- (ii) Age group mortality.

But it is difficult to imagine a physical basis for the difference in appendicitis mortality between Scotland and England and Wales.

### SUMMARY

1. Appendicitis was given a separate line in the tables in the Annual Reports of the Registrar General for Scotland for the first time in the report on 1901.

2. Between 1901 and 1945, 17,701 deaths from appendicitis were registered in Scotland. Of these 156 were registered in 1901, 257 in 1945.

3. The mean annual mortality rate per 100,000 for the whole period is  $8.19 \pm 1.68$ . The annual rates range from 3.49 in 1901 to 10.51 in 1923.



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The unique soothing properties of Angier's, its favourable influence upon assimilation and nutrition, and its general tonic effects, make it eminently useful both during and after influenza. It has a well-established reputation for efficiency in relieving the troublesome laryngeal or tracheal cough, correcting the gastro-intestinal symptoms and combating the nervous depression and debility.

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1 oz. Bemax provides approximately :—

vitamin B <sub>1</sub>	0.45 mg.	vitamin E	8.0 mg.	protein	30%
vitamin B <sub>2</sub>		manganese	4.0 mg.	available carbohydrate	39%
(riboflavine)	0.3 mg.	iron	2.7 mg.	fibre	2%
nicotinic acid	1.7 mg.	copper	0.45 mg.	calorific value	104
vitamin B <sub>6</sub>	0.45 mg.				

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TABLE B

*Distribution of Population and Deaths from Appendicitis by Sex and Age Groups in Three Census Years in Scotland*

Age Group	1	Males.						Females.					
		2	3	4	5	6	7	8	9	10	11	12	13
		1911.						1921.					
		Census Population.	Registered Deaths.	Census Population.	Registered Deaths.	Census Population.	Registered Deaths.	Census Population.	Registered Deaths.	Census Population.	Registered Deaths.	Census Population.	Registered Deaths.
0-4 .	.	268,158	10	238,587	21	213,598	9	264,587	6	233,786	10	209,748	6
5-9 .	.	257,900	32	240,161	40	229,401	19	255,858	27	237,185	29	226,312	24
10-14 .	.	246,763	39	246,627	47	214,547	24	243,371	34	243,366	35	211,268	12
15-24 .	.	435,214	48	441,751	57	424,954	63	447,004	41	465,130	58	435,915	40
25-34 .	.	352,222	29	327,466	21	348,793	26	389,054	16	386,812	24	389,735	24
35-44 .	.	290,723	29	295,944	31	278,366	31	309,687	23	336,564	14	339,031	26
45-54 .	.	213,458	18	261,275	31	256,588	28	233,232	17	273,225	20	290,528	32
55-64 .	.	139,048	12	172,410	18	207,228	28	156,822	12	189,536	18	222,564	35
65-74 .	.	78,299	9	91,650	11	114,121	24	106,687	4	115,229	7	140,872	16
75 and over .	.	26,868	1	31,398	5	37,837	7	45,570	3	53,631	2	60,414	8
Totals .	.	2,308,653	227	2,347,269	282	2,325,433	259	2,451,872	183	2,534,464	217	2,517,387	223

Note.—The group "age not stated" is excluded from the population statistics as deaths in this group were not registered in any of the three above years.

4. On arranging the statistics of population and deaths in four decades and a final group of five years (1941-45), the first decade is heterogeneous, the second and third homogeneous, the fourth heterogeneous, the last five years homogeneous. In the fourth decade the years 1931-37 form a homogeneous group in which the mortality rate does not differ significantly from the mean rate in the decade 1921-30. The last six years 1940-45 also form a homogeneous group.

5. With the exception noted in (4) the mean rates for these homogeneous periods differ significantly from one another.

6. The mean death rate per 100,000 for the 1901-10 is 6.30 for the last six years, 1940-45, is 5.90. The mean rate for 1931-37 is 9.41. After 1937 the rates drop until the homogeneous rate for the last six years is reached. From 1911-30 the decade rates increased from 8.8 to 9.8 per 100,000; the drop to 9.41 for the years 1931-37 is insignificant.

7. Mortality from appendicitis is higher in Scotland than in England and Wales.

8. Mortality from appendicitis is higher for males than females.

9. Both in Scotland and in England and Wales in 1931 age and death rates are positively and significantly correlated. This correlation becomes insignificant for Scotland, and the significance is reduced for England and Wales, on holding population constant.

10. The correlation coefficient between age and mortality rates in Scotland does not differ significantly from that for England and Wales.

11. The highest mortality rates (15 per 100,000) are found in 1931, the last census year, in the age groups over 55. In the same year the lowest rates (7.2) are found in the age groups up to 15. Intermediate rates (9.8) are found in the central age groups 15-55.

12. The rates in this central age group 15-55 show insignificant differences between the three census years 1911, 1921, 1931. In the highest age groups, 55 and over, the rates in 1911, and 1921 do not differ significantly but the rates in 1931 are significantly highest. In the lowest age group female rates are homogeneous in the three census years; the rates for males and both sexes rise in 1921 and fall in 1931.

The writer is indebted to Mr J. G. Kyd, Registrar General for Scotland for his kindly permission to study the records in Register House; to Messrs. J. Tupman and T. Gardiner for their help in collecting the data; to Dr R. S. Barclay for Diagram 1; to Professor A. C. Aitken for helpful advice; to Miss M. T. Craig for her accurate typing from the manuscript.

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# SYMPOSIUM ON HEADACHE AS A SYMPTOM

## I. SOME GENERAL CONSIDERATIONS \*

By W. A. ALEXANDER, M.B., F.R.C.P.Ed.

Physician, Royal Infirmary, Edinburgh

HEADACHE is probably the commonest of all symptoms and yet the problem is one which has not been much discussed in open session. In this Society, which has now been in existence for a century and a quarter, it is only from the ocular standpoint that it has been previously considered. This leads me to remark that the idea of tonight's discussion originated with our President, Dr H. M. Traquair, who has long pled for a more critical attitude to the problem. As he is one of the few amongst us who combine in a notable way the scientific and the philosophical outlooks, and as the subject is one which calls for such treatment, I regret that he is not the opening speaker, but his wish was that the approach should be a more general one and that he himself should concentrate on the ocular aspect.

The disinclination on the part of the profession, which I have postulated, to formulate its ideas on headache is easily understood. The task is one of great complexity and raises considerations, on many of which there is no consensus of opinion, which are fundamental in the realms of anatomy, physiology and psychology, not to mention general medicine and psychiatry, so that the ordinary doctor, whom I represent, may be excused for feeling overawed by its magnitude. I suspect also that he has the uneasy feeling that the years have not increased his comprehension of the problem in any material way or at any rate have not enabled him to deal with it in practice, except in certain directions, any more effectively than did his forefathers, and that therefore silence is the better part. There is some truth in this, but it would be a surprising thing if, with the wonderful developments in the surgery of the brain which we have been privileged to witness and with the stimulus provided by the great clinical investigators and assessors of modern times, such as Mackenzie and Lewis in this country, along with that deeper understanding of the mind which I think we can claim has occurred, there had not been any increase in knowledge in this direction. Such is of course the case, as some of this audience who were present at a Guest Lecture in the Department of Surgery some two years ago by Professor Jefferson of Manchester, will confirm. Most of the recent work has been concerned with the mechanism of headache and, as might be expected, a good deal of it has emanated from America. At this point, I may be allowed to express the earnest hope that Mr Norman Dott may be persuaded

\* Read at a meeting of the Medico-Chirurgical Society of Edinburgh on 7th May 1947.

to review for our benefit the subject of headache and also in due course to present a clinical analysis based on the incomparable records of his department.

It is necessary to our theme and of great interest to refer to the structures at the head level which are sensitive to pain. It seems that the calvaria (without its periosteum), the brain itself, and most of the dura and pia-arachnoid are insensitive; and that the investing tissues on the outside of the skull, the basal dura with its tentorial shelf, and the blood vessels are sensitive. It is this latter point which demands emphasis, the sensitivity of blood vessels at this level. The cranial arteries, particularly in the territory of the fifth nerve, which include the extra-cranial arteries such as the temporal, the dural arteries such as the middle meningeal, and the cerebral arteries, in addition to the great venous sinuses and their tributaries from the surface of the brain, seem to be highly sensitive to distension, traction and pressure. All arteries in the body are in some degree sensitive, but it has to be assumed, I think, that the cranial arteries are peculiarly so. In some ways this sensitivity may be bound up with the fact, which we must also accept, that the cerebral arteries are more important than any other arteries, in the sense that they subserve tissue which is of all tissues the most vital and the most susceptible to oxygen deprivation. I should like to add, when on the subject of the individuality of cerebral arteries, though it may not be relevant to the issue, that these arteries have always struck me as being structurally different from other arteries. They have thinner walls, are more collapsible and presumably more distensible than arteries elsewhere, and indeed look like veins. Moreover, pathologically, they are more liable to the patchy form of arterial degeneration, atherosclerosis, than other arteries of comparable size, with the possible exception of the coronaries. It may also be the case that this segment of the circulation reacts exceptionally in the pharmacological field. This somewhat lengthy reference to these blood vessels is justified by the importance now attributed to them in the mechanism of headache.

The all important nerve in respect of our subject is of course the fifth, but below the level of the tentorium pain impulses are also conducted by the ninth and tenth cranial nerves and the upper three cervical nerves. These nerves are implicated in headaches in general but, needless to state, if they are directly involved in any local lesion, pains of special distribution will result. The rôle of the cervical sympathetic, if any, in relation to headache must be left unresolved. Likewise, I shall make no attempt to discuss cephalic pathways and reception stations.

To deal now briefly with the question of the mechanisms of headache, it is surprising to learn that, in cases associated with increased intracranial pressure, the degree of headache bears no relationship to the height of the pressure and that extreme pressures may be artificially induced without producing headache. On the other hand,

a drop in intracranial pressure is usually productive of headache, as is commonly found after lumbar puncture, especially it is believed if the opening in the dura and arachnoid is large enough to allow of seepage after the withdrawal of the needle. The mechanism naturally differs with the underlying cause, but what it is important to emphasise is that opinion has hardened in the direction of the recognition of a vascular basis for most headaches. Even in the case of tumour, with its alteration of stresses and shifts, the emphasis is on traction on, and tension of, the pain-sensitive vascular structures. A possible exception is in the case of the headache of meningitis in which some chemical product of the local inflammation may directly irritate the pain receptors.

The important part played by cranial arteries in the genesis of headache was first suspected in the case of migraine, and I well remember Professor Edwin Bramwell supporting and elaborating the vascular thesis in a paper on "Migraine" in the Section of Neurology at the annual meeting of the British Medical Association in 1926, a viewpoint which I may say received little support in the subsequent discussion, but which time has confirmed. I recall also having my attention drawn to the paper by Pickering and Hess which appeared in 1932, in which the headache produced by the intravenous injection of histamine was described and analysed, an observation which was the starting-point of much subsequent work at home and abroad. Histamine is of course a potent vaso-dilator substance, and there seems to be ample proof that the headache produced by it is due to the stretching of cerebral arteries. This is an example of a biochemical substance acting directly on the vessel walls, and a similar type of action might be expected to operate in the clinical group of headaches loosely called toxic; at any rate pyrexial headache has much the same character as histamine headache.

It is to be noted that the headache in migraine—and this evidently holds good also for the headaches experienced by hypertensive subjects—is related particularly to the extracranial arteries and especially the temporal, *i.e.* to branches of the external carotid, whereas the artificial histamine headache and the naturally-occurring pyrexial headache are the result of effects mainly on the cerebral arteries, *i.e.* on branches of the internal carotid and basilar. This focal action—and even more so the unilateral distribution of many migrainous headaches—is most puzzling and I offer no explanation. One thing which strikes me about the arterial thesis is that, if headache is to be explained merely on the basis of distension and increased amplitude of pulsation of cranial arteries, it is a matter of some surprise that disturbances of the general circulation characterised by the dancing of arteries, such as aortic incompetence and severe thyrotoxicosis, should not be marked by headache more constantly than they are.

To turn now, rather belatedly, to clinical incidence, I shall attempt no definition of headache. Time does not allow of a reference to

points in the analysis of head pain which may be of significance in diagnosis, such as character, situation and times of occurrence, and in any case I could not draw profitable deductions. There is no really satisfactory method of classification of headaches, and I must be excused if I discuss the subject further on the basis of those questions which I put to myself in any case of headache the nature of which is not soon obvious.

1. *Does the explanation lie within the skull in the shape of some organic change?* I do not propose to elaborate this. Theoretically, it should not be difficult, if time be taken over the history and the examination, and an intelligent use made of the ophthalmoscope, to decide this point, though localisation may be impossible, but in practice the diagnosis of cerebral tumour, especially if it be supratentorial, may be a matter of great difficulty, and I need hardly say that tuberculous meningitis in its early stage may be one of the most treacherous of diseases. The frequency and importance of syphilis as a cause of headache used to be impressed upon us, but there has been a great change in this respect. Traumatic headache has become more common, even apart from the wars, but its consideration would require an evening to itself.

2. *If the cause does not lie within the skull, does it then rest in the bones themselves or in their coverings?* Others will be dealing with certain aspects of this question, and I shall content myself with raising one point and that is the difficulty of deciding whether pain in the back of the neck is of intracranial or extracranial origin. There was described by Cabot what he called "indurative headache," a type of occipital headache which he ascribed to fibromyositis of the trapezius, involving one or other of the occipital nerves. He regarded it as common. Then I remember Dr Risien Russell at Queen's Square suggesting that rheumatism of the scalp and occipital muscles was a fruitful cause of headache. My own mind is not clear on this score, and I should welcome an expression of opinion from others.

3. *If the cause of the headache be not local, i.e. does not lie inside or outside the skull, can it be related to a physical cause elsewhere in the body?* There are innumerable possibilities, and many are obvious, such as the various toxic substances, intrinsic or extrinsic, which are known to produce headache. I shall refer only to certain factors, and first hypertension. I have already said that hypertensive headache resembles migraine in respect of mechanism, and have to add, which is within the experience of us all, that headache in hypertensive subjects does not parallel the rise in blood pressure. That being so, it is not easy to offer a satisfactory explanation for the occurrence of headache in hypertension, but it seems likely that it is the more emotional hypertensives who are liable to headache, i.e. those who were apt to suffer from headaches prior to the development of their hypertension, and perhaps these are persons with some instability of vasomotor tone.

I might mention also the frequent occurrence of headache in women in relation to menstruation. There seem to me to be three possible explanations of this association: (1) that the headache is a reflex one, *i.e.* mediated through nervous connections, (2) that a hormonal influence acts through the blood directly on the cranial arteries, and (3) that a temporary disturbance of the balance of the endocrine complex results in swelling of the pituitary and tension on the sensitive dorsum sellæ; but I am unable to suggest which is the most likely.

On the subject of constipation as a cause of headache, I should like to say that I am not convinced that there is such a close association as is claimed. Were it so, patients with chronic obstruction from carcinoma of the distal colon might be expected to complain of headache more frequently than they do; as might those who are found to be harbouring a faecal mass in the rectum. In any case, I believe it to be a good thing that less is being heard of intestinal toxæmia as a cause for headache.

Anæmia is mentioned in the textbooks as a common cause of headache, but this is not my experience.

With regard to another cause, which has a place in the older textbooks, it interested but puzzled me to read in the transactions of this Society that the late Sir George Berry in a communication in 1909 on "Eye-strain" wrote: "One not very uncommon cause of headache, with which I have met in cases referred to me . . . is *gout*. In adults this cause is not likely to be overlooked, but it is much more frequently missed in children." Now, I wonder what he had in mind when he made that statement, in Edinburgh of all places, where gout is virtually unknown.

4. *No adequate physical explanation being forthcoming, must the headache be regarded as psychogenic or psycho-somatic in origin?* I believe that most headaches met with in practice come into this category. It often seems as if they become a habit or, perhaps, conditioned reflex. Again, leaving migraine out of consideration, one is tempted to recognise an inherent liability or diathesis to headache. It is certainly true that some fortunate people go through life without experiencing a headache except for some very definite physical cause, whereas others, not always clearly neurotic, seem to be constantly afflicted.

It is of interest to ask whether it is the impression of the more senior practitioners that headache is a less frequent complaint than it was. There are reasons, I believe, why this should be so, chief amongst them being the emancipation of women-folk and the adoption of a more sensible type of dress, but other stresses and strains have arisen of recent years which may have had a counteracting effect.



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# SYMPOSIUM ON HEADACHE AS A SYMPTOM

## II. MIGRAINE\*

By JAMES K. SLATER, M.D., F.R.C.P.Ed.  
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READING through a random selection of my notes of cases classified as migraine one observes the same phrases recurring again and again both in the history and in the description of the patient :—

"Life would be perfect had I not inherited the miserable tendency to sick headaches."

"After all the worry of making preparation I cannot trust myself to be present when the occasion arises," dinner party, meeting, or whatever it might be. Anticipation seems to bring on an attack.

The afflicted individuals have much in common, liker to each other than to their own sister. They are described as alert, bright, intelligent, conscientious, energetic, with obviously high standards of conduct, yet withall æsthetic, suggesting an easy fatigueability which some admit and others wont. My impression, supported by these notes, is that the vast majority are women, yet it is often stated that men are frequently victims, but if this is so they seem either less incapacitated or more stoical since, in my experience, they seldom seek advice. On the other hand, in army work during the war, numerous soldiers were so labelled with no other justification than that they had become tiresome complainers of headache of one sort or another in the Unit M.I. Room. "All headache is not migraine, and all migraine is not headache" is a dictum too often forgotten. That phrase hits at the core of the problem and stimulated my interest in the subject some twenty years ago when a patient, demanding full investigation, stated to me that even if I cured her headache she would still be far from well since in her view it was the liver or the stomach which was primarily at fault. In these days, as I shame to remember, the routine procedure following a negative physical examination, was to invoke the aid of biochemistry, X-ray, any and all the methods of precision, until eventually some local abnormality might be revealed, and so it happened that they, these earlier victims, were deprived of an appendix, gall stones, ovary, septic teeth, without alas a favourable effect on the presenting complaint. There is seldom, if ever, any need to put these people through the whole diagnostic mill. The story with its limited variations, the type of individual, and on occasion, if thought necessary, the therapeutic test, will

\* Read at a meeting of the Medico-Chirurgical Society of Edinburgh on 7th May 1947.



diagnose correctly 99 out of 100 of them. A very different malady is disseminated sclerosis, yet in this as in migraine it is the pattern, recognisable from case to case, that makes of it an entity. What then are these several well-established criteria upon which we may depend? Most can speak of other members of the family similarly encumbered; their personal story of irregularly recurrent headache goes back probably to early adolescence. They emphasise a fairly well-defined prodromal stage in which there are present various and variable symptoms of accumulating toxæmia, such as malaise, irritability, inability to concentrate, the development of pallor, and feelings of chilliness, disturbance of appetite and digestion, and occasionally a feeling of false stimulation with restless excitable tension states. The incapacitating headache stage usually follows some hours later and is described as one-sided, mostly frontal and temporal at first, and spreading to the whole of the head and into the occiput or back of the neck. Nausea is usually present and vomiting occurs in about half the cases. Eye symptoms, such as blurring, scotomata, fortification spectra, and "neon" signs occur just before or during the headache stage in 20 per cent. of the cases. The whole affair is over in twenty-four to forty-eight hours, seldom longer. A stage of elimination is often described by the patient and, in most instances, is characterised by rapid elimination of urine. Local soreness lasts for a time. Relief or improvement following injection of ergotamine tartrate is another criterion for diagnosis in many cases.

This represents the typical case the proportion of which varies greatly in the reports of different authors but, broadly speaking, the higher the total the larger is the percentage. Alvarry and Palmer each quote over 500 cases and show that 60 to 70 per cent., or even more, are pretty true to type; other authors with smaller totals vary much more. But however great the variation there is always sufficient of the pattern to make the diagnosis certain.

Classification has for long been unsatisfactory. Migraine appears in the literature as psychoneurosis, vaso-motor neurosis, sometimes as an allergic intracranial œdema, and always spoken of by the average layman as a "sick headache" or a "bilious headache," but the great amount of accumulated research has made considerable strides towards elucidating the mechanism involved.

I must dispose of the vast themes of causation and therapy in very few words, leaving it to the discussion to bring out special points. Gone are the days of the mid-twenties when I was set the task of measuring the opening of the entrance and broadest diameter of the sella turcica, comparing those of migraine subjects with others, inspired by the enthusiastic writings of Timme and others. Periodic headache of pituitary origin does occur, but it is not migraine. The migraine subject has inherited something more subtle than a capricious endocrine. It must surely be some basic idiosyncrasy or constitutional

tendency, and this acts as a precipitating factor when a suitable emotional stress or tension exists. The latter alone is obviously insufficient, otherwise the migrainous population would be gigantic. Complete proof exists that the painful phase commences when there is a localised vaso-dilatation of the cerebral capillaries and arterioles, most often branches of the external carotic artery on one side, later spreading and being associated with a variable amount of cerebral oedema, all this visible externally as flushing, pulsation, and being tender to touch. Much weighty evidence is available to show that, in many instances, this is a form of allergy in a susceptible individual. Establishment of the entity "histamine headache" has helped to throw light on vascular headaches and, although it is readily distinguishable from true migraine, yet the mechanism in this stage of the cycle has many features in common, at least they both have the feature of vaso-dilatation. The rôle of allergy in this complaint is thorny and difficult, but it deserves, and has received a great deal of attention. Can it be, as seems attractive, that in the candidate the necessary tension so upsets the vaso-motor control of the gastrointestinal tract as to allow the offending molecule to be more readily absorbed when in fact it happens to exist?

Migraine is a tormenting, and at times agonising complaint, but now with a growing understanding of the matters involved many cases should be benefited more than they are, and it is no answer to pile up lists of forbidden foods, any more than it is advisable to make her dependent upon a variety of analgesics or sedatives. Ergotamine, or perhaps the new American Octin, cuts short many existing attacks, but they are relatively useless prophylactically, and in no sense a "cure." It is here that the art of medicine should be seen at its best, since at an early age it is possible to spot the potential victims and, by advice and guidance, so order their lives in such a way as to prevent the full development of a symptom-complex that is apt increasingly to become irreversible.

# SYMPOSIUM ON HEADACHE AS A SYMPTOM

## III. PSYCHOLOGICAL ASPECT \*

By W. M. C. HARROWES, M.D.

CERTAIN complaints demand scrutiny of both complainer and his setting. Headache is often one such.

All living creatures must, in order to continue to live, either dominate or adapt to their environment. In this connection we have to abandon any attempt to conceive environment as having physical properties or limits. Obviously the internal milieu of tissue fluid so carefully kept constant in the process of homeostasis and the external milieu mesh in with each other at secreting and absorbing surfaces, but apart from that what we would have to call environment would be every sort of event calling for adaptation or offering a challenge for domination. Some time ago in a search for definition, a fact was defined as something that made a difference; in this sense environment is a set of facts of diverse quality and of positive and negative value.

Man's adaptive capacity has been enormously raised above that of other mammalia as a result of the great development of connector material between the very large sensory inflow and the relatively small motor outflow, the so-called final common path through which, however, all that we can ever do must ultimately pass. In its highest form this connector material has assumed the capacity of segregating stimulus from response, first of all in association with the distance receptors—eye and ear—and then as a manifestation of our unique symbolising function in terms of image as primary symbolisation, and speech as secondary symbolisation. It is this symbolising capacity of language as the palæontology of mind operating with more or less consciousness and hanging together in a flow of meanings constituting a biography and a life pattern which is our adaptation mechanism par excellence bringing, as it does, past, present, and estimates of future all together as if they were present now and ready for scrutiny by the subject.

The adaptations so sponsored are widely spread and elaborated in contrast with adaptations where stimulus and response have not been segregated by the symbolising function to produce mentally integrated behaviour. The question of pain shows this up well. Animal forms seek to break off contact with items which would harm them even when it is doubtful if anything like mind is present.

The brainless frog pushes away the paper wet with acid, the spinal dog with insentient limbs will hold up a pricked foot and run away

\* Read at a meeting of the Medico-Chirurgical Society of Edinburgh on 7th May 1947.

with the other three. These are protective mechanisms and in both cases there is no pain, but their importance for survival is of the highest. When, however, such stimuli of a potentially dangerous nature become connected with "minding" as Sherrington says, their sensual accompaniment is rich in affect in emotion which amplifies and reinforces the measure of protection and relief the pure reflex act affords, and furthermore the time element is different. Unlike the purely immediate reflex, mentally integrated pain is organised into the time system of the subject as unpleasant and not to be repeated. Physical pain is the response of the total organism to what would otherwise merely stimulate a protector reflex. The local reflex affords its limited protection, but the mental event of pain produces or attempts to effect an appropriate reaction of the whole organism.

We have then, general adaptive mechanisms and problems and responsibilities, and the special adaptive technique of pain.

The everyday vocabulary of pain is enormous and interesting, and hardly requires more than passing mention for it is so well known. Such and such a person, and such and such a thing give us a pain we say, because we wish to avoid them, and headache is no exception. In America for years and now in this country, a "headache" has come to mean a worry or a problem for the good reason that everybody knows quite well that worries and problems do produce headaches in many people. It may even be that the common phrase "a pain in the neck" may indicate the occipital and nuchal pains so commonly associated with prolonged worry.

Now, it is a commonplace and nobody knows it better than we do, for we see it every day that humans, if they have a pain in a certain locality assume that there is something wrong there. Pains in the chest are heart disease, pains in the back are kidney disease. Pains in the head are brain disease or something of the kind. The plain man has pretty clear-cut views about this. He believes that the brain is the mind, and he feels that he must not overtax his brain or his mind because if he does so then it will get tired or maybe give up altogether or begin to misfire somehow and he will go mad. He believes that using his mind is a good thing, but you can have too much of it, and when he finds that he is being forced to think in a way that taxes his general adaptive capacity beyond a certain point then the fear which always follows any threat to adaptive capacity is engendered. The general adaptive capacity in terms of minding is a question of foresight, and when the foresight becomes "fearsight" then, as you all know, certain vegetative phenomena are produced which in many cases lead to head pains. I should like to make it clear that in a great many cases, however, nothing of the kind occurs and the reaction to general adaptive strain takes the form of some other stress in some other part of the individual. The headache having been produced at any rate, the individual then reacts to it as well as to the situation which has evoked it, and intellectual elaborations of all

kinds take place so that the whole nexus of the headache becomes a completely individual reaction in terms of all the assets and liabilities of the individual and his general philosophy of life and his setting.

The association of rest and pain is a classic and, of course, head pains appearing in this way are as a rule interpreted by the subject as having the meaning of a call for rest of the thinking function, and one hears this expressed every day. "I had such a headache that I could not think," is a common phrase. It usually means "I had such a headache that I felt I ought to stop thinking." But of course the individual, especially in the circumstances, cannot stop thinking and the headache goes on.

Clinically every type of psychiatric reaction may show headache at times as a symptom, most frequently prodromal. The complaint disorders (the neuroses), the bizarre reactions of the schizophrenic paranoid group, the mood disorders, the toxic disturbances and the acquired organic deficit conditions all may show this symptom.

The neuroses, forming as they do about one third of all cases appealing for medical aid, are naturally the group that is most significant for the everyday practice of medicine.

In many cases the story of head symptoms in the neurotic follows a rather regular course. At first, under the weight of adaptive strain, headache is experienced, supratentorial or infratentorial in origin, then comes a peculiar event sometimes known as the psycholeptic attack. This consists of a sudden snap or bang, apparently inside the head as if something under tension, like a piece of elastic, had given way. One patient whom I saw recently said she thought at first it was a boy near her firing a toy pistol. The effect of this experience on a person already concerned about his adaptation, his brain and mind, can be well imagined. It usually produces extreme fear and distress which leads to the really typical head symptoms of psychiatry, not headache but odd head sensations. These are absolutely innumerable sensations inside the head, often slightly painful but chiefly troublesome on account of their oddness and the fear of brain and mind disorder which they carry. They consist of such things as feelings of weight, pressure of a foreign body, of woolliness—and these are often associated with depression and anxiety—feelings of trickling, crackling, bubbling, turbulence and so on endlessly. Their affective nature is well shown by their better response to sedatives than to analgesics. The other day there was a woman of sixty-three who for twelve years had had "turmoil" in her head following a psycholeptic attack which in turn had followed several years of headache and worry. She was only able to lie in a darkened room. A pentothal narcosis was carried out, and for two hours after it she had no symptoms whatever.

As a contrast I might mention a woman of thirty-six who kept house for her widower father. He married again and she was very unhappy. She developed headaches and finally a depression with some persecutory ideas. The headaches were frontal and very severe.

But it turned out that when Mr Dott exposed the supraorbital branches of her trigeminal he found that each notch was a foramen pressing on the nerves which were thus irritated.

One might also mention a man of thirty who was knocked down by a train in terrifying circumstances and sustained a depressed fracture of the vault where operation had left a large deficiency in the skull allowing us to carry out some of the early experiments on brain volume during sleep. It occurred to us, however, to try the effect of hypnosis on the severe headache he had. Recreation of the accident in hypnosis intensified the headache and appeared, as far as our rough methods went, to be associated with increase in brain volume. Suggestions in hypnosis in the contrary direction obliterated the headache for a time.

In regard to this symptom, I think I can hardly do better than quote the words of my old chief, Adolf Meyer, when he said, "If we obey our soundest instincts we study events far less for their absolute nature than in order to learn the conditions under which they arise and under which they can be modified."

## SYMPOSIUM ON HEADACHE AS A SYMPTOM

### IV. THE EYES AND HEADACHE \*

By H. M. TRAQUAIR, M.D., F.R.C.S.E.

ANOMALIES of the eyes, especially refractive errors, are regarded as a frequent cause of headache, but opinions as to their importance in this respect differ widely. Estimates varying from 80 to 10 per cent. have been advanced from time to time; the tendency in recent years has been towards the lower percentage which I find is in accordance with my own clinical experience.

The effects of the eye conditions concerned are known as "eye strain," a term which has no exact significance and no scientific meaning. It is assumed that the muscles of the eyes are "strained" although no evidence of any pathological change in them has ever been demonstrated. Everyone is familiar with the expression "strain" as applied to the muscles of the heart or limbs when they are called upon to do more work than they can undertake without discomfort or damage. The eye muscles respond to demands for extra output by hypertrophy in the same way as other muscles and thus equilibrium is attained.

Ocular headache occurs, however, irrespective of the use made of the eye muscles. It is absent, for example, in the hypermetropic squinter, who affords the most pronounced example of over-exertion of the eye muscles both for accommodation and for convergence, and may be present in low myopes who make relatively small demands upon their eye muscles, especially upon the ciliary muscle on which the blame is mainly cast. On the other hand high myopes, who habitually over-exert their internal recti in order to produce the high degree of convergence they require, may suffer from discomfort owing to the necessity to hold reading matter so close but do not usually complain of headache.

It is also noticeable that eye headaches are nearly always related to the use of the eyes for near work, rarely in connection with distant vision except in cinemas, in which a rapidly moving picture is presented to the eyes.

Persons who see with one eye only or with one eye at a time, that is to say those who have not binocular vision, are not troubled with ocular headache in spite of the popularly accepted view that the seeing eye must be undergoing "strain" because it "does all the work." It is because he sees with only one eye that the squinter, who uses his muscles so strongly, escapes headache. While he foregoes the advantages of binocular vision he avoids the burden of co-ordinating his eye muscles in the effort to procure it.

\* Read at a meeting of the Medico-Chirurgical Society of Edinburgh on 7th May 1947.

Vision may be good or bad, there is no definite relationship. Unequal vision in the two eyes, as long as the vision of the worse eye is not bad enough to exclude it from participation in the combined vision of the two eyes, may be associated with headache.

Headache may be present in the absence of refractive error. A fruitful cause of headache is so-called "muscle imbalance," by which is meant faulty alignment of the eyes. Vision may be excellent but there is difficulty in co-ordinating the muscular action of the two eyes so as to bring them both to bear on the same point. It is the difficulty of driving two horses as compared with one, especially if the two are not well matched.

The focussing muscles, the intrinsic muscles, and the directing muscles, the extrinsic muscles, work together as a co-ordinated neuro-muscular mechanism in the interest of binocular vision. A refractive error is very apt to throw this mechanism out of gear. If the achievement and maintenance of binocular vision are not made more difficult headache is not likely to be caused whether refractive error is present or not, and if binocular vision is difficult headache is caused irrespective of the presence of refractive error. In one-eyed persons the question does not arise and headache is escaped. The refractive error *per se* does not cause headache and the expression "eye strain" should be regarded as meaning "strain" in a figurative, not a literal, sense as one might say "frayed nerves."

How should an opinion be formed as to whether a headache is of ocular origin or not? The answer is: By the study of the type of headache. The presence of refractive error associated with headache in any given case does not necessarily mean that the headache is caused by the refractive error. Therefore, it does not seem desirable to approach a case of headache by an ophthalmic examination in order to "eliminate the eyes," or to search for and correct any "ocular element" which may be present before making a diagnosis. This is the method of eliminative diagnosis, or diagnosis based upon the collection of reports, as opposed to constructive diagnosis which is based upon the study of the patient. If the headache is of ocular type and if refractive error such as is likely to produce headache is also present a causal connection may be assumed. If glasses are advised merely because a refractive error is discovered many patients will wear spectacles—as they do now—unnecessarily and uselessly. Nearly every eye has some form of refractive error which can be corrected by lenses, but these errors are not necessarily productive of headache. Sometimes, however, the oculist finds himself obliged to order spectacles as a psychotherapeutic measure and, if prescribed with assurance, they do good in suitable cases if only for a time.

In examining the symptomatology of ocular headache the age, sex, domestic environment and occupation are taken into account. Ocular headaches are common in young adults who have much near work to do, and more common in females than in males. The position,



character, periodicity and duration of the pain are important features. The pain may be described as being behind the eyes or in the temples, sometimes in the occiput, rarely in the vertex. It is not generalised, or limited to one side as in migraine, or localised as in supra-orbital neuralgia. It is usually of a dull aching character and the more severe it is the less likely it is to be of ocular origin. "Terrible," "splitting," "bumping," "throbbing," "bursting," or prostrating headaches are not ocular (except in acute eye disease), nor are those brought on by stooping. The headaches are usually definitely related to work and are relieved or cease at week-ends and during holidays. They do not interfere with sleep.

The general condition of the patient is often an important determining factor. A healthy robust young person can overcome a refractive error which might cause headache in another. Constipation, anæmia, overwork, or insufficient rest may reduce resisting power and thus act as adjuvant causes of headache. Of great importance is the mental factor. Many patients are neurotic, hypersensitive and suggestible, and every ophthalmic surgeon sees many headache cases in which domestic maladjustment of one kind or another is present. A clinical impression is that a large proportion of female patients seen in ophthalmic practice on account of headaches have a psychogenic basis for their symptoms.

The treatment consists in the use of suitable spectacles to relieve any difficulty in the way of achieving and maintaining efficient binocular vision. In all cases it is necessary to examine and treat the patient and not only the eyes.

## SYMPOSIUM ON HEADACHE AS A SYMPTOM

### V. HEADACHE FROM SINUS INFECTIONS \*

By A. BROWNLIE SMITH, M.D., F.R.C.S.E.

Assistant Surgeon, Ear, Nose and Throat Department, Royal Infirmary,  
Edinburgh

IN a small popular textbook on diseases of the ear, nose and throat there are indexed no less than 41 conditions which produce headache, ranging from a foreign body in the nose to a cerebral abscess. As it is quite impossible to discuss all these in the time available, I propose to confine my remarks mainly to headache as a symptom of disease of the nasal accessory sinuses.

(1) Headache is a frequent symptom of infection of the nasal sinuses; (2) It may occur in the presence of some lesion of the sinuses and yet bear no relation to that lesion, and (3) It may occur from a sinus lesion without that lesion being discoverable.

An acute or chronic infection of the nasal sinuses may cause headache but this headache varies according to the sinus or sinuses which are mainly affected. An infection of the frontal sinuses produces a headache which is usually very typical; it varies in intensity throughout the day, it commences about ten o'clock, becomes often so severe in the middle of the day that the patient feels he wants to hit his head against the wall to obtain relief; it passes off in the afternoon and usually does not return until the following morning. If the headache does not begin until the afternoon, one often finds that the patient's habits are irregular. Recently a young girl was admitted to the Infirmary with an acute frontal sinusitis, but the headache did not appear until two or three o'clock in the afternoon. Her occupation was that of a dancer at the Palais and she did not get out of bed until after lunch. Patients on night duty have the headache during their hours of work. The intense headache of malaria may be easily confused with that of frontal sinusitis and, in a case I saw recently, the diagnosis presented some difficulty as, although the patient had served in India for some time, his first attack of malaria occurred after he had been demobilised.

An infection of the sphenoidal sinuses produces a headache which is more marked over the vertex or in the occipital region and sometimes shows the same diurnal variation. An infection of the ethmoidal cells causes pain behind the eyes and in the temple. It is necessary to remember also the "lower half" headache which has been described

\* Read at a meeting of the Medico-Chirurgical Society of Edinburgh on 7th May 1947.

by Sluder. This is due to vaso-motor changes in the affected areas as the result of reflexes set up by irritation in the region of the sphenopalatine ganglion. The headache is usually preceded by slight coryza and, on examination, an infection of the posterior ethmoidal cells or an empyema of the sphenoidal sinus may be discovered. Pain begins at the root of the nose, around the eyes, and extends backwards to the temple, then to the mastoid region and to the occiput and back of the neck. There is often a point of maximum tenderness about five centimetres behind the mastoid process.

I think that there is still some doubt whether maxillary sinus disease produces headache or not. It certainly causes considerable pain and aching in the face, but I remember the late Dr J. S. Fraser telling me that maxillary sinusitis did not cause headache. So often does one see patients, who have a severe infection of the maxillary antrum from which much foul smelling pus can be obtained, who never complain of headache at all. It is possible that the toxicity which arises from the presence of enclosed pus may cause what has been called a toxic headache.

Generally speaking, an infection of the nasal sinuses produces a fairly typical headache and evidence of this infection can usually be found on clinical or radiological examination.

A real problem arises when some lesion of the sinuses is discovered, usually on radiological examination, in a patient who suffers from an unexplained headache. The headache is usually frontal in distribution, is not typical of a true sinus headache, and the lesion found is often a slight opacity of the ethmoidal cells or an opacity of the floor of the maxillary antrum. In these cases one should as far as possible take steps to exclude definitely any infection in the sinuses but, at the same time, try to prevent the patient being given a peg—sinusitis—on which to hang perhaps a psychogenic headache. I should imagine that there is nothing more satisfying to a physician, who has a patient suffering from recurring unexplained headaches, than a positive radiological finding in the nasal accessory sinuses. Bateman, a rhinologist in the R.A.F. during the war, found that in 34 per cent. of his sinus cases he failed by sinus treatment to cure or alleviate the headache from which they suffered and attributed the failure in these cases to the fact that the co-existence of sinusitis and headache did not necessarily mean that the latter was due to the former. I was acutely aware of this in the Middle East where headache was a very frequent complaint and the majority of my out-patients were referred to me with a diagnosis of sinus headache. Occasionally one found slight radiological changes in the sinuses but rarely did one find definite clinical evidence of a real infection, and I observed that posting to the home establishment was a more effective remedy than any operative treatment to the sinuses. When one so often sees a patient whose nasal cavities are completely filled with nasal polypi, or whose maxillary antra are filled with pus and who never has a complaint of

headache, one finds it difficult to understand why a slight opacity in the floor of the antrum should produce this symptom.

The third type of case is that in which the headache resembles a sinus headache and yet no clinical or radiological evidence of sinusitis is found, although the headache really arises from some affection of the sinuses. At one time, vacuum frontal headache was a common explanation of the pain which arises over the frontal sinus, and of the tenderness which can be elicited by pressure over the floor of the frontal. But I observe that, while a whole page is allotted to the condition in the 1926 edition of Logan Turner's book, it receives little more than a few lines in the more recent edition. The occurrence of a vacuum in the sinus is difficult to explain in the absence of marked changes in air pressure around the patient. If, under normal pressure, a progressive swelling of the lining of the sinus has closed the ostium, then any further swelling will produce a positive pressure rather than a negative one. By the same mechanism, swelling of the mucous lining of the sinus may force part of the enclosed air out of the sinus cavity and later, still in the presence of a blocked ostium, a partial vacuum might result when the œdema and vascularity of the lining of the membrane diminishes. Much information on the occurrence of headaches resulting from changes in air pressure in the nasal sinuses has been obtained by R.A.F. surgeons and, during the war, the occurrence of sinus barotrauma was fairly frequent. McGibbon, however, found that positive radiological findings were present in 75 per cent. of cases; hæmorrhage into the sinus, œdema and hæmorrhage of the lining membrane, and serous exudation were common findings. But these changes occurred when the patients were exposed to very marked changes in the surrounding air pressures. One is impressed by the fact that, even when, as in the R.A.F., the members of the services are exposed to conditions which produce marked changes in the pressure in the nasal sinuses, the R.A.F. rhinologists regarded many of the headaches occurring in the personnel as psychiatric in origin.

There is one other point I would like to mention. I have for some years occasionally seen young people, about the age of puberty, complain of pain over the mastoid process. Otological examination has been completely negative but X-ray examination has often shown very extensive pneumatization. One gained the impression that the actual physiological development of the mastoid cells, at a time when that development would normally be ceasing, was sufficient to produce, if not severe pain, at least sufficient discomfort to draw the attention of the patient to the part. One wonders if a similar condition does not also occur in the accessory sinuses. Although I have no facts to give, it would be interesting to know if the headache from which the schoolboy or schoolgirl complains in the latter part of school life is not due to the actual physiological development of the nasal accessory sinuses.

## DISCUSSION

*Professor D. K. Henderson* opened the discussion by expressing thanks to those who had taken part. The subject was a difficult one and further help and guidance were necessary. It was interesting to hear the question tackled from the different points of view. Professor Henderson was particularly interested in Dr Brownlie Smith's presentation of the subject in connection with the different types of sinus infection.

It was essential, Professor Henderson considered, to exclude all possible organic reasons for headache before referring the patient to the psychiatrist and he appealed for greater co-operation in dealing with this difficult problem—only by so doing could further progress be made.

*Dr John Gillies* said he found it a little difficult to accept the explanation by Dr Alexander and Dr Slater of vaso-dilatation as a mechanism of pain. The pain related to blood vessels, he thought, was more usually associated with vaso-constriction. Vaso-dilatation of a limb was not associated with pain—why then was pain caused by vaso-dilatation of the cerebral arteries?

*Dr Traquair* referred to the homonymous character of the teichopsia in migraine, and asked Dr Slater and Dr Alexander whether this did not indicate involvement of the internal carotid artery which supplied the visual path.

*Drs J. K. Slater and A. Brownlie Smith* answered suitably.

# OBITUARY

ROBERT ALEXANDER FLEMING  
M.A., M.D., C.M., LL.D., F.R.C.P.E., F.R.S.E.

DR FLEMING was a physician of wide culture and a characteristic product of Scottish education. Born in Dundee, he received the greater part of his training in Edinburgh. After taking the Arts course, he graduated M.A. in 1884 and turned his attention to medicine. A distinguished undergraduate career culminated in the award of first-class honours when he took his M.B., C.M. in 1888. He acted as resident physician to Professor Grainger Stewart and subsequently held every post available to him in the Royal Infirmary, being successively tutor and clinical assistant, pathologist, assistant physician, physician and consulting physician. His M.D. thesis in 1896 was awarded a gold medal. On the outbreak of war in 1914 Dr Fleming was mobilised as a Captain in the 2nd Scottish General Hospital at Craigleith, and later with the rank of Major accompanied the unit to Salonica where he had charge of the medical division of the hospital.

He was one of the first to be appointed a Senior Lecturer in clinical medicine, and for many years acted as secretary of the Clinical Board with a seat in the Faculty and membership of the Senatus Academicus. When he retired from active service in the Infirmary the University honoured him with the degree of LL.D.

Dr Fleming took a great interest in the welfare of the Royal College of Physicians and served it in many ways. He was a member of Council from 1923 to 1927 and again from 1931 to 1933, President 1928 and 1929, and Vice-President in 1930. He was for many years one of the Trustees of the College, and at various times he represented the College on the Committee of Management of the Triple Qualification, the Governing Board of the School of the Royal Colleges, the Board of the Dental School, the University Settlement and the Council of Social Services.

Dr Fleming's professional life did not cease on his retirement from the Royal Infirmary in 1927, for he continued to act as Physician to the Edinburgh Hospital for Incurables. He was also medical adviser to the Prison Commissioners, a post which brought him into contact with crime and criminals and gave him material for his Morison Lecture in 1933. His sympathetic and understanding handling of Borstal boys will be long remembered.

Dr Fleming was an active member of many professional and learned Societies, including the Edinburgh Medico-Chirurgical Society of which he was at one time President. He was a member of the King's Bodyguard for Scotland and for many years was surgeon to the Royal Company of Archers.

A man of wide training and critical judgment, Dr Fleming was essentially a teacher. For some years he gave a course of lectures on medicine in the Extra-Mural School, and he published *A Short Practice of Medicine* which ran to three editions. As a clinical teacher his kindly personality, his gift of exposition and his careful technique attracted many students. Medical education was a subject ever near his heart, and he did everything in his power to forward the interests of the Edinburgh School, both University and extra-mural.

Though he had many interests, his love for his profession remained till the end, and after practising for nearly sixty years he died at his country home at Innerhadden, Kinloch Rannoch, on 6th December 1947 at the age of eighty-five.

## NEW BOOKS

*Ethics for Modern Nurses.* By KATHERINE A. DENSFORD, M.A., R.N., and M. S. EVERETT, PH.D. Pp. x+260. London: W. B. Saunders Company. 1946. Price 9s. net.

This book was written to enable the young nurse to make a satisfactory adjustment to her new surroundings and to help her to formulate a workable philosophy of life. It aims at teaching basic principles rather than specific rules of conduct. It might also serve as an introduction to a study of social science. The book is admirably written, it contains a vast amount of common sense and should satisfactorily fulfil the purpose for which it is intended.

*Early Ambulation and Related Procedures in Surgical Management.* By DANIEL J. LEITHAUSER. Pp. x+232, with 36 illustrations. Springfield, Illinois, U.S.A.: Charles C. Thomas. 1946. Price \$4.50.

To anyone interested in the practice of early ambulation after surgical operations this monograph will be invaluable. The reflex functional disturbances which follow abdominal operations, and which the author describes as the laparotomy syndrome, are described, and the causes and prevention of post-operative complications—respiratory, circulatory, gastro-intestinal, etc., are very fully discussed. The author describes the technique he has adopted and deals with the type of incision, method of wound closure, anaesthesia, pre- and post-operative treatment, etc.

The advantages claimed are early restoration of well-being and activity, a striking absence of post-operative complications of all kinds and a greatly shortened sojourn in hospital.

The results quoted are impressive.

*Year Book of Neurology, Psychiatry and Neuro-Surgery.* Edited by HANS H. RUSE, M.D., MABEL G. MASTEN, M.D., NOLAN D. C. LEWIS, M.D., and PERCIVAL BAILEY, M.D. Chicago: The Year Book Publications. 1946. Price 21s. net.

This is a most valuable annual compendium of information, regrouped this year by the substitution of Neuro-Surgery for Endocrinology, a reflection of the changing ideas of specialisation and obviously a more convenient arrangement. Those who are accustomed to using this book await its publication each year with eager anticipation, since they have long learned to depend on the insight with which its subject matter is chosen. Present-day restrictions in this country make one's wait tantalisingly long, yet patience is rewarded in the remarkably convenient form in which so much valuable information is made available. An excellent index and some hundred-odd carefully selected illustrations add to the attraction that this moderately priced volume will always have.

*A Practical Handbook of Psychiatry for Students and Nurses.* By LOUIS MINSKI, M.D., F.R.C.P., D.P.M. Pp. 128. London: Wm. Heinemann, Medical Books, Ltd. 1946. Price 6s. net.

A book of this size must be extremely difficult to write owing to the necessary amount of compression. In this instance it is so sketchy and so lacking in practical detail that it fails in its purpose, and could not possibly be satisfying either to students or nurses even for the mere purpose of passing examinations. Furthermore, many of the dogmatic assertions which are incorporated are misleading and open to severe criticism; for instance, that "insulin shock therapy has completely altered the outlook in schizophrenia." Would that it were so.

*Anatomical Terms: Their Origin and Derivation.* By E. J. FIELD, M.D., M.S., and R. J. HARRISON, M.A., M.B., B.CHIR. Pp. 165. Cambridge: Heffer. 1947. Price 7s. 6d. net.

Within the limits mentioned by the authors in the Preface, this little book should prove a valuable aid to most medical students in the understanding of anatomical terminology. It is perhaps unfortunate that, in a few cases, confusion may arise because special connotations are obscured (e.g. "chyle" and "chyme" both appearing simply as "juice"); while other derivations are expanded with detail irrelevant to the purpose.

The book, which is well set forth and of a convenient size for pocket reference, is a useful addendum to a standard medical dictionary.

*Current Therapies of Personality Disorders.* Edited by BERNARD GLUECK, M.D. Pp. v+200. London: William Heinemann Ltd. 1947. Price 17s. 6d. net.

The series of papers comprising this book were presented at the Annual Meeting of the American Psychopathological Association in 1945. The contributions were thought to present such a combined whole that they have been brought together in this particular way. All of the contributions reach a very high standard indeed, and give a very good idea of psychiatric practice and treatment as it is developing to-day. In addition, however, and even more importantly, the general belief is expressed that the psychiatry of the future will exercise a greater influence on world affairs. It is refreshing to find all of the material presented in a well-reasoned and moderate manner. This is a book which can be recommended.

*Physical Treatment of the Injuries of the Brain and Allied Nervous Disorders.* By K. M. HERN, M.C.S.P., DIPL. OF L.P.T.C. Pp. iii+94, with 34 illustrations. London: Baillière, Tindall & Cox. 1947. Price 10s. 6d. net.

The ultimate aim of all physiotherapy is restoration of function. This statement may seem a platitude, but in his foreword to this volume Sir Charles P. Symonds emphasises the often overlooked attention to detail which, in fact, is the justification Miss Hern has in setting forth her unique experiences and the methods she has so successfully developed.

Naturally much use is made of photographs and these are excellent, which, coupled with the emphasis laid upon a proper balance of all the factors in a given case, the physical and psychological, the social and economical, make the real value of the work. To all who are interested in rehabilitation and occupational therapy this study, emerging from extensive personal experience, will make a ready appeal as a pattern to follow.

*Bovine Tuberculosis, Including a Contrast with Human Tuberculosis.* By JOHN FRANCIS, B.Sc., M.R.C.V.S. Pp. 220, illustrated. London: Staples Press Ltd. 1947. Price 25s. net.

This book contains a great deal of information about tuberculosis in the bovine. The information is drawn from many sources and is presented in a well documented form. It makes interesting reading, particularly from the point of view of comparative pathology, for those interested in the human disease, and for the veterinarian it provides an exhaustive discussion of bovine tuberculosis and the pathological and administrative problems which it entails. The reference section contains a list of 411 publications which alone are a tribute to the work which the author has brought to bear on its production and which are of great value to those wishing to secure more detailed information. The book is written in an easy style. The author, even in his statistics, is never tedious, but it is a pity that in places the writing is marred by bad punctuation and impossible sentences which are not in keeping with the general excellence of the work.



## NEW EDITIONS

*Anatomy of the Nervous System.* By S. W. STEPHEN, M.D., PH.D. Eighth Edition. Revised by SAM L. CLARK, M.D., PH.D. Pp. 532, with 417 illustrations. London: W. B. Saunders Company. 1947. Price 32s. 6d. net.

In this new edition the order of presentation has been altered to some extent, new textual material and illustrations have been added and various parts have been rewritten. A key-note of the whole work is the interpretation or significance of physiologic changes in nervous disease, a particularly interesting feature to remark upon in view of the chosen title, showing as it does the closely integrated concept of this branch of medicine.

It goes without saying in a work that has already passed through so many editions, that all recent research has been carefully evaluated and given its due place in the whole, but while the clinical illustrations are useful they naturally make no claim to be exhaustive.

Without undue discrimination in reviewing a volume so balanced and informative, it may be said that the bibliography, which spans over half a century, will be found particularly valuable more especially to research workers in neurology.

*Modern Methods of Feeding in Infancy and Childhood.* By D. PATERSON, B.A., M.D., F.R.C.P., and J. FOREST SMITH, F.R.C.P. Ninth Edition. Pp. 184, with 13 figures. London: Constable & Co. 1947. Price 8s. 6d. net.

The appearance of a further edition of this well-known book is evidence of its popularity and usefulness.

It was hoped that with the cessation of war, rationing would cease and a return to peace-time standards become possible, but this has not been realised, and austerities are still necessary. The book describes in detail the feeding of the normal child at all ages and also gives the modifications required for various types of illness.

This is a book which should be in the hands of every practitioner of medicine.

*Surgical Applied Anatomy.* By Sir FREDERICK TREVES. Eleventh Edition. Revised by LAMBERT RODGERS, M.Sc., F.R.C.S., F.R.C.S.E., F.A.C.S., F.R.A.C.S. Pp. xxxii+529, with 192 illustrations. London: Cassell & Co. Ltd. 1947. Price 20s.

This little manual of surgical anatomy which has been in existence since 1883 amply maintains Sir Frederick Treves' object in compiling it—"to assist the student in judging the comparative value of the matter he has learnt."

The text is arranged on a regional basis, it is lucid and delightfully readable and the illustrations, while in places being rather cramped, are on the whole good.

The book should not only be of great value to the senior student in helping to revise his anatomy but also to correlate this with the basic principals of surgery, as such it can be thoroughly recommended.

*Pasteurisation.* By HARRY HILL, F.R.SAN.I. Second Edition. Pp. viii+296, with 73 illustrations. London: H. K. Lewis & Co. Ltd. 1947. Price 21s. net.

The second edition of this excellent handbook which is well illustrated, describes from an essentially practical point of view modern techniques for the efficient heat treatment of milk with a view to rendering it safe for human consumption. In the reviewer's opinion the value of the work would have been enhanced if the author had included a chapter on the specific problems of the education and training of semi-skilled and unskilled labourers concerned in the handling of milk in large modern dairies.

*Sociology and Social Problems in Nursing Service.* By GLADYS SELLEW, B.S., R.N., PH.D. Second Edition. Pp. xv+379, illustrated. London: W. B. Saunders Company. 1946. Price 14s. net.

Social factors play a considerable part in the problems of individual patients and may influence their reactions to treatment and their adjustment to disability. Application of the information presented in this book should enable the nurse to acquire an insight into the social aspects of human nature and personality and should help her increase the value of her service to her patients.

The problems discussed are based almost entirely on American experience but the general principles are universally applicable.

*Food Inspection Notes.* By H. HILL, F.R.SAN.I., and E. DODSWORTH, M.R.SAN.I. Second Edition. Pp. viii+126. London: H. K. Lewis & Co. Ltd. 1947. Price 6s. net.

The second edition of this small book follows the same lines as the "Aids" series and has been prepared for students training to be food and meat inspectors. With the changing emphasis of the new D.P.H. regulations the appeal of this work to purely medical readers must be strictly limited, all the general principles involved being adequately dealt with in any textbook of Hygiene which they are likely to use.

*Hey Groves' Synopsis of Surgery.* Edited by SIR CECIL P. G. WAKELEY, K.B.E., C.B. Thirteenth Edition. Pp. viii+637, with 13 plates and 193 other illustrations. Bristol: John Wright and Sons Ltd. 1947. Price 25s. net.

This new edition should prove invaluable to the undergraduate. The book is well arranged, subject matter largely unequivocal, type and illustrations clear, and index extensive. Although there is a chapter on recent chemo-therapeutic substances, a note of their administration in the treatment sections of various conditions is frequently omitted.

*Biochemistry for Medical Students.* By W. V. THORPE. Fourth Edition. Pp. vii+496, with 36 figures. London: J. & A. Churchill Ltd. 1947. Price 18s. net.

The latest edition of Dr Thorpe's textbook covers the same wide field as the previous editions, and the subject is equally clearly expounded. It is a general textbook in every sense, and its information is reliable and concise.

It incorporates many recent advances in biochemistry, and includes a new, but unfortunately short, chapter on isotopes and their uses.

Errors are few and unimportant.

*Psychology Applied to Nursing.* By L. A. AVERILL, PH.D., and FLORENCE C. KEMPF, A.M., B.S., R.N. Third Edition. Pp. xv+496, with 55 illustrations. London: W. B. Saunders Company. 1946. Price 12s. 6d. net.

The earlier part of this book follows standard lines; the later emphasises the application of psychology in a nursing career. It has been planned to make it easy for the nurse to apply what she learns about human behaviour to the practical problems of her work.

The authors, an educational psychologist and a registered nurse, have collaborated to produce a most useful book.

*A Guide to Anatomy.* By E. D. EWART. Sixth Edition. Pp. xii+318, with 119 illustrations, 35 coloured including 55 plates. London: H. K. Lewis & Co. Ltd. 1947. Price 25s. net.

This new edition of Miss Ewart's book has been brought up to date by introducing the revised terminology, and by the revision and addition of many illustrations, including fifty plates. It is now a much more valuable book. It is not sufficiently detailed to be considered a complete textbook for students of physiotherapy for

whom it was originally intended, but it can be considered an excellent introductory and reference book. A number of recent questions set in the examinations of the Chartered Society of Physiotherapists, the Society of Occupational Therapists and the Society of Radiographers are given in the appendix. It is well produced, with a generous number of clear diagrams and plates, on good paper and with clear printing.

*Recent Advances in Pathology.* By G. HADFIELD, M.D., F.R.C.P. and L. P. GARROD, M.A., M.D., F.R.C.P. Fifth Edition. Pp. viii + 363, with 60 illustrations. London: J. & A. Churchill Ltd. 1947. Price 21s.

During the five years since the appearance of the fourth edition there have been some remarkable advances in knowledge. In consequence it has been necessary to re-write the chapters on diseases of the liver and also of the kidney. Other new matter relates to experimental cancer, inflammation, silicosis and the site of antibody formation.

This book maintains the high tradition of the *Recent Advances* series.

## BOOKS RECEIVED

- BOWER, ALBERT G., A.D., M.S., M.D., F.A.C.P., and PILANT, EDITH B., R.N.  
Communicable Diseases for Nurses. Sixth Edition.  
(*W. B. Saunders Company, London*) 20s.
- CAWADIAS, A. P., O.B.E., M.D., F.R.C.P. Clinical Endocrinology and Constitutional Medicine . . . . . (*Frederick Muller Ltd., London*) 42s. net.
- CHRISTOPHER, FREDERICK, B.S., M.D., F.A.C.S. Minor Surgery. Sixth Edition . . . . . (*W. B. Saunders Company, London*) 60s.
- Edited by COMPERE, EDWARD L., M.D., F.A.C.S. The 1947 Year Book of Orthopedics and Traumatic Surgery.  
(*The Year Book Publishers, Chicago*) \$3.75
- COOPE, ROBERT, M.D., B.SC., F.R.C.P. Diseases of the Chest. Second Edition.  
(*E. & S. Livingstone Ltd., Edinburgh*) 25s. net.
- CUTTING, WINDSOR C., M.D. A Manual of Clinical Therapeutics. A Guide for Students and Practitioners. Second Edition. Illustrated.  
(*W. B. Saunders Company, London*) 25s.
- ENGLISH, Sir CRISP, K.C.M.G., F.R.C.S. Diseases of the Breast.  
(*J. & A. Churchill Ltd., London*) 8s. 6d.
- FRAZER, W. M., O.B.E., M.D., CH.B., M.SC., D.P.H., and STALLYBRASS, C. O., M.D. (State Medicine), CH.B., D.P.H., M.R.C.S., L.R.C.P. Text-Book of Public Health. Twelfth Edition.  
(*E. & S. Livingstone Ltd., Edinburgh*) 30s. net.
- Edited by GREENHILL, J. P., B.S., M.D., F.A.C.S. The 1947 Year Book of Obstetrics and Gynecology . . . . . (*The Year Book Publishers, Chicago*) \$3.75
- JENKINS, WILLIAM DAVID, J.P., B.A. (HONS.) (WALES), M.R.C.S., L.R.C.P. Dermatoses among Gas and Tar Workers.  
(*John Wright & Sons Ltd., Bristol*) 25s.
- KINSEY, ALFRED C., POMEROY, WARDELL B., and MARTIN, CLYDE E. Sexual Behavior in the Human Male . . . . . (*W. B. Saunders Company, London*) 32s. 6d.
- MANDL, FELIX, M.D., F.I.C.S. Paravertebral Block.  
(*William Heinemann (Medical Books) Ltd., London*) 32s. net.
- MCDONACH, J. E. R., F.R.C.S. The Universe in the Making. A Biochemical Approach . . . . . (*Messrs Chatterson Ltd., London*) 7s. 6d. net.
- MUTEHAM, WILFRED A., M.P.S. How to Become a Pharmacist.  
(*The Actinic Press, London*) 5s.
- O'CONNER, WILLIAM A., L.M.S.S.A. (LOND.), D.P.M. (LOND.). Psychiatry: A Short Treatise . . . . . (*John Wright & Sons Ltd., Bristol*) 35s. net.
- SARGANT, WILLIAM, M.A., M.B. (CANTAB.), M.R.C.P., D.P.M., and SLATER, ELIOT, M.A., M.D. (CANTAB.), F.R.C.P., D.P.M. An Introduction to Physical Methods of Treatment in Psychiatry. Second Edition.  
(*E. & S. Livingstone Ltd., Edinburgh*) 10s. 6d. net.
- SOLLMANN, TORALD, M.D. A Manual of Pharmacology and its Applications to Therapeutics and Toxicology. Seventh Edition.  
(*W. B. Saunders Company, London*) 57s. 6d.
- STOCKINGS, G. TAYLEUR, M.B., B.S., D.P.M. The Metabolic Brain Diseases and their Treatment: In Military and Civilian Practice.  
(*Baillière, Tindall & Cox, London*) 16s. net.
- WRIGHT, HELENA, M.B., B.S. Sex Fulfilment in Married Women.  
(*Williams & Norgate Ltd., London*) 5s. net.

# Edinburgh Medical Journal

April 1948

THE FOUNDER OF THE MEDICO-CHIRURGICAL  
SOCIETY OF EDINBURGH \*

VALEDICTORY ADDRESS

By THE PRESIDENT, H. M. TRAQUAIR, M.D., F.R.C.S.E.

TO-NIGHT I take leave of you as your President, and in so doing it is my duty to say farewell in the form of a Valedictory Address.

In the past such addresses have varied in length from a few words to the monumental record of Handyside in 1872, marking the fiftieth anniversary of the Society, which occupied over sixty pages of the *Edinburgh Medical Journal*. This Jubilee Chronicon, as it was later styled by Caird, is, however, a valuable historical document in the annals of the Society as it gives a full account of its activities during the first fifty years of its existence.

On this occasion it seems fitting that the names of the forty-six members who died during the six years between 1939 and 1945 should be placed on record. Some, such as Professor Gulland and Sir Norman Walker, who were members for fifty-three and fifty-one years respectively, were giants in the medical world whose fame extended far beyond the Edinburgh Medical School. Familiar personalities, such as Chalmers Watson, an enthusiast on nutrition; William Fordyce, distinguished as a gynæcologist and famous for his songs; W. T. Ritchie who followed Gulland in the chair of medicine and made a name for himself as a cardiologist; John Comrie who did so much for the history of medicine; and W. A. Cochrane to whose work in orthopædics the school owes so much, have gone from us. In Robert Thin and David Huskie we lost two fine examples of the general practitioner of the old type, whose like the future organisation of medical practice seems unsuited to encourage. D. Stewart Middleton and J. J. M. Shaw, both not only surgeons of the first rank but also men of exceptional quality, and H. W. Dryerre died on active service. We also lost E. F. Armour, J. J. R. Binnie, A. Hill Buchan, May L. Cameron, J. B. Cunningham, John M. Darling, J. M. Dewar, D. Elliot Dickson, Alexander Goodall, Stewart Hodgson, John Jamieson, H. G. Langwill, W. C. McEwan, A. Morrison McIntosh, Malcolm

\* Read at a meeting of the Medico-Chirurgical Society of Edinburgh on 5th November 1947.

McLarty, Douglas McRae, J. Hally Meikle, Kenmure Melville, W. T. Munro, J. McNair Murray, H. Oliphant Nicholson, G. Keppie Paterson, C. M. Pearson, J. Hogarth Pringle, A. G. Ritchie, William Robertson, T. W. E. Ross, James Scott, Robert Somerville, Robert Stewart, Robert Stirling, A. Pirie Watson, A. Murray Wood, and W. W. Wood. All were cherished colleagues whose memory will help us to endeavour to maintain their standards. Some members have left us to occupy important posts elsewhere, but in the last two sessions sixty-three new members have joined the Society so that our numbers are fully maintained and, together with an excellent balance-sheet, give sound evidence of sustained popularity and prosperity.

The papers contributed attained a high standard and members who had been abroad on war service gave their experiences.

The most important feature of the Society's work has been the consideration of a proposal to associate the medical societies of Edinburgh together with this society and form a new integrated sectionalised society with combined sectional meetings to discuss subjects of common interest. This movement, which may be regarded as an indication of the health and vitality of the Society, was initiated by Professor Bramwell last November in an important paper on "The Evolution Function and Scope of the Medical Society," and discussions are still going on with the object of evolving a practical scheme. Another important event was the combined meeting with the Medico-Chirurgical Society of Glasgow held in March of this year. Those of us who attended were most hospitably entertained, and an interesting debate took place on the motion "That the Nation is tending to become Disease-Conscious rather than Health-Conscious," which was carried by a considerable majority. I may remind you that in virtue of a resolution passed by the Glasgow Society in 1843 and reciprocated by ourselves, members of either society may attend meetings in Edinburgh or Glasgow without introduction. It is to be hoped that further combined meetings may be held, the next in Edinburgh.

The subject matter of previous valedictory addresses, whether long or short, has frequently been historical. This is not surprising, for the historical approach has a real value for the practising physician. It has, indeed, been said that the history of medicine in its relationship to the development of medical thought, is the highest scientific method in medicine. Moreover, the history of a subject is like digging for treasure, although much has been done the feeling always remains that something of interest or value may still await discovery. It is also of interest to note how many ideas, schemes and projects, which engage our attention at the present time, were conceived many years ago only to end in stillbirth because the conditions necessary to make them viable were not yet in existence.

With the exception of the address by Joseph Bell in 1894, who referred to the future of the Society, no address ventured upon the

future of Medicine, and here the retiring Presidents exhibited no doubt a wise and prudent, though one may think a regrettable, caution, for it would have been intriguing had any of them hazarded his imagination.

During the 125 years of its existence, this Society has seen more changes in medical thought and practice than in the 1400 years between Galen and Harvey. These changes have been developing with ever-increasing rapidity, most of them having taken place during the last seventy years, and it becomes daily more evident that they are merely the precursors of an evolution even more vital and more wonderful.

This Society was founded in what may be called the budding period of modern medicine. At the time of its birth, scepticism and rebellion were beginning to replace the old attitude of respect for authority; there were no less than eighteen scientific societies in Edinburgh, and doctors thought themselves, and liked others to think them, scientific.

Although the origin and early history of the Society have often been dealt with in previous addresses, I propose to-night to give you a somewhat more detailed sketch of the medical life of our founder—unfortunately we know nothing of his personal life—and of the Edinburgh of his time.

About the year 1790 Andrew Hamilton, Deputy Comptroller of Excise in Scotland, settled in Buccleuch Place, then a recently built and fashionable suburb. As he was only thirty-six years old at the time, he must have been an able man to have attained such an important post. He died in 1796 leaving four young children. His widow survived him for fifty-two years, so that the two boys, Robert and John, were brought up under her care and without the advantages of a father's guidance. Robert, the second son, was born in 1794, two years before his father's death, and became the founder of our Society. His brother John, a year younger, became a member of the Faculty of Advocates, but died at the age of fifty-two. The other two died young.

At this time Edinburgh was slowly emerging from its mediæval condition. The Tolbooth, defended by the Town Guard with their Lochaber axes, and the Luckenbooths still jammed up the High Street at St Giles. The North and South Bridges had been completed for a few years, but the New South Bridge, or George IV Bridge as it was afterwards named, was not yet begun, and the nostrils of the neighbourhood were still assailed by the stench of the candlemakers' boiling tallow. Geordie Boyd's Mud Brig, later called the Earthen Mound, was taking form across the swamp which is now Princes Street Gardens, but was far from finished. At night the streets were dimly lit by sparse oil lamps, for gas was not introduced until 1820, when a beginning was made in the High Street with cockspur burners. The population, including that of Leith, numbered about 100,000, of whom some 7000 lived in the New Town, thirsty and unwashed according to Cockburn, as the water supply was not only insufficient but had to be carried, often up high stairs, either by the householder

himself or by a "water-caddie." Sedan chairs or hackney chairs, as they were then called, were hired from the Tron Church. The fare to Buccleuch Place was ninepence, to Charlotte Square two shillings.

The names of John and Robert Hamilton appear in the class lists of the Royal High School from 1804 to 1807, and although there is no conclusive evidence that they were Andrew Hamilton's sons, we may imagine the two boys trotting down the hill together from Buccleuch Place to the old building in the south-east angle of the Flodden Wall near the Surgeons' Hall and the old Infirmary. The school was then in the height of its fame in the last years of the erudite and scholarly Dr Adam. School instruction in Edinburgh at that time was almost entirely classical, and Robert was probably taught little beyond Latin and a modicum of Greek, in which subjects he would, however, be much better versed than the medical student of to-day. There is no record of where or how he received the finishing touches to his general education during the next two years. He evidently determined from the beginning to equip himself fully for his profession and entered upon his work in the College of Surgeons and the University at the same time. In June 1811, at the age of seventeen, he became apprenticed to John Abercrombie, to whom he afterwards referred as "my honoured master." The apprenticeship was part of the College training. It lasted for four years and the indenture had to be discharged at a meeting of the College before the diploma was granted. Hamilton was one of a group of young men who received tutorial and practical instruction in surgery and medicine in Abercrombie's private out-patient clinic, a method of teaching introduced by Abercrombie himself. In the same year he entered the University, the Toun's college. The splendid new building, the pride of cultured Edinburgh, was slowly and fitfully rising—it was to take forty-five years to complete—and, although the foundation-stone had been laid five years before Hamilton was born, was barely half built when he entered as a student; on the south side the building was incomplete, exposing the quadrangle with the library, an old dilapidated building, in its north-eastern corner.

Young Hamilton lost no time in getting to work. In 1812 he joined the Royal Medical Society, of which he was to become a president four years later. He took a prominent part in the activities of the Society and read four dissertations, one on the nature of headache and another on asphyxia, which later became the subject of his M.D. thesis. He received his diploma from the College and his M.D. doctorate from the University both in 1815 at the age of twenty-one.

At that time the University required a minimum of three years' study, and the curriculum consisted of classes in botany, chemistry, anatomy, theory and practice of medicine, clinical medicine and *materia medica*. The more enthusiastic students, of whom Hamilton was evidently one, used to supplement this course by including some voluntary subjects such as obstetrics and clinical surgery and prolonged

their studies to four years. Discussions with the professors took place but no class examinations or periodical professional examinations, as we know them to-day, were required. The final test consisted of comments on one or two aphorisms of Hippocrates, oral examinations conducted in Latin, and a medical thesis written and orally defended in the same language. The oral examinations were held at the house of one of the professors, where the faculty met for the purpose, and the candidate might be questioned on any of the five subjects by any of the professors as there was no specialisation. Hamilton's thesis was entitled "De Asphyxia." After graduation he spent five years away from Edinburgh, mostly in London and Dublin, where he held hospital posts, and partly in Vienna and Germany.

On his return in 1820 he settled in Northumberland Street and was evidently received with open arms by his colleagues. In the same year he became a Fellow of the College of Surgeons, his probationary essay submitted for examination being "On some diseases reputed venereal." In 1821 he became surgeon to the Magdalene Asylum and his experiences there led to the publication in 1823 of a paper on the influence of panic in the propagation of contagious disease which, no doubt, reflected the influence of Abercrombie as a psychologist. In the same year he was elected a member of the Harveian Society, whose presidential chair he occupied in 1829, and of the Æsculapian Society, and a Fellow of the Royal Society of Edinburgh. In the following year he became an original member of the Medico-Chirurgical Club, which was formed on his own suggestion to be a "social meeting free from the alleged stiffness of some other clubs." It was to meet on Thursday nights to discuss the Society meeting of the previous evening over a light supper of finnan haddock, spatchcock and beer. He also became a vice-president of the short-lived Phrenological Society, a medical officer to the New Town Dispensary, and an examiner to the College of Surgeons. Of his connection with the New Town Dispensary all the information we possess is contained in a few lines in the "*Nugæ Canoræ Medicæ*" of Douglas Maclagan, who was the Poet-Laureate of the Dispensary, which contain a reference to Hamilton's travels in Europe :—

There was Watson  
And Hamilton,  
A chap—but that's no matter—  
Who had gone to spy  
How folks mind their eye,  
On the other side o' the water.

Hamilton was evidently a man of enquiring and original mind and must have been regarded as a "lad o' pairts," for he was not yet thirty when these distinctions were showered upon him. While not a prolific contributor of medical and ophthalmological papers, and rarely speaking at meetings of the Society, he was a man of wide interests. He wrote on natural history subjects such as "*The Amphibious Carnivora*,"



on whales, and a two-volume book on *The Natural History of British Fishes*.

In the work of the College of Surgeons Hamilton took an active part. For three years before the appointment of Dr Knox as conservator in 1827, he was one of the keepers of the museum and contributed much to its early development.

Although in his probationary essay for the fellowship of the College he had referred to "venereal ophthalmia," Hamilton does not appear to have devoted himself to ophthalmology until later. In 1841 he was appointed one of the two surgeons to the Edinburgh Eye Infirmary, then in Elder Street and now in Cambridge Street, and in 1843 he published an important paper in the *Edinburgh Medical Journal*, in which he lamented the backward state of ophthalmological teaching in this country, the need for clinics, and especially the absence of any professorship in the subject. It is interesting to note that nearly a hundred years were to pass before the first professorship in ophthalmology in Britain was established, and that in Glasgow, not in Edinburgh.

In December 1846, just one hundred years ago, Hamilton became President of the Society. It may be relevant to his career that he was not the choice of the council who favoured Dr Beilby. Apparently the Society elected Hamilton; Beilby became the next president. On his assumption of the Chair, in one of the most interesting addresses ever presented to the Society—the subject was Homeopathy—Hamilton describes its birth. In response to his appeal, which he called a "requisition paper," fifty-three names were speedily obtained as "requisitionists." \* No one refused. Hamilton does not mention that he received help from any of his colleagues in forming the Society, but it is evident from the account given by Handyside that John Gairdner and William Brown were actively associated with him. At the first meeting on 16th May 1821 only private business was conducted. Dr Duncan, senior, was elected President, and Hamilton one of the two secretaries. Hamilton points out that it was his experiences in London and Dublin which stimulated him to action, and that in making his appeal he endeavoured to avoid any tendency to "party" influence—a consideration which could not affect us at the present time—and that he specially approached the younger members of the profession "because in that sphere it was to be presumed that there would be more elasticity and energy, and less fear perhaps of jarring and discrepancy." He was himself only in his twenty-sixth year. The Society was to open an "ample door" to the profession and to be "in no degree sectional." As for its object he states: "Our Society aims at one object alone, the improvement of our science for the public benefit and our own that we may be the better fitted to discharge

\* Hamilton states in his address that he had with him the original requisition paper and would hand it to the Society for preservation. A search in the archives of the Society has failed to discover any such document.

our high duties." I think it may be claimed that the Society has laboured unremittingly and with no small measure of success to fulfil the aspirations of its founder.

The first meeting for Public Business took place in December 1821, and the first paper was one by John Abercrombie on the pathology of the heart.

In the early days of the Society, owing to the almost complete absence of specialisation, its activities were widely spread. In addition to purely medical and surgical contributions, papers on chemical, physical, zoological, literary and philosophical subjects were presented. Nor was the Society silent in matters of more general public interest; in 1853 it presented petitions to both Houses of Parliament in relation to medical reform.

After his presidential address little more is recorded of Hamilton's work. In the College of Surgeons he served on the museum committee between 1844 and 1848 and on the President's council from 1851 to 1853. In 1847 he recorded a case of imperfect vision from irregular refraction, and his last publication, "The True Scriptural Sabbath Vindicated," appeared in 1854. He ceased to sign the reports of the Edinburgh Eye Infirmary after 1857, but remained on its staff until 1866, two years before he died.

Quite early in his career, about 1830, a cloud seems to have come between Hamilton and the sun. In that year he resigned the secretaryship of the Society and his membership of the Medico-Chirurgical Club and of the Æsculapians, and next year his membership of the Harveians, and he seems to have withdrawn himself to a great extent from general medical work. There is some evidence that he tried to establish himself as an ophthalmic specialist, for he changed his designation from "surgeon" to "physician and oculist," and in 1850 his professional address was 140 George Street, the address of the Edinburgh Eye Infirmary, while he lived at Sciennes House. He wandered about Edinburgh and ultimately moved to Merchiston, where he died in 1868, leaving a widow who died in 1879. He appears to have had no children, and with his death almost the whole of Andrew Hamilton's descendants became extinct. His grave is in the burial-ground of his father in the graveyard of the West Kirk, known to us as St Cuthbert's, and, though the monument bears an almost fulsome eulogy of Andrew Hamilton, Robert's name is merely recorded as one of the children.

Hamilton's early promise of becoming a prominent member of the medical profession in Edinburgh does not seem to have been fulfilled. In his endeavour to become a specialist he was probably before his time. His death received a merely casual mention in the annals of the Society, and no obituary notice was published. It is curious that this man, who founded our Society and did so much for the establishment of ophthalmology in this school should have been allowed to slip away as quietly and modestly as he had lived. In taking leave of

Robert Hamilton we may surely accord him a more generous tribute than the half-hearted praise of Handyside, who could find nothing better to say of him than that he was "an estimable man and a teacher of ophthalmology in this school." Surely, however, the words of Christopher Wren could not be more apt: "If you wish to see his monument look around you." It is for us to ensure that it remains more enduring than brass.

Before closing this sketch of the earlier days of the Society, mention may be made of some of the more interesting advances in medicine and surgery introduced by its members.

The use of silkworm gut in surgery was first advocated in 1825, not for sutures but for the ligature of vessels, in a paper by John Fielding.

In November 1847 Sir J. Y. Simpson read his memorable paper on "A New Anæsthetic Agent."

The hypodermic syringe was first used in Britain in 1853 and submitted to the Society two years later by Alexander Wood. His syringe was made in Edinburgh and originally designed for the injection of aneurysms with perchloride of iron.

In 1857 the battle of blood-letting was fought out on the floor of the Society and won by Balfour and Hughes Bennet, who delivered the death-blow to exsanguination as an "antiphlogistic" measure.

In 1863 Argyll Robertson introduced eserine, already described by Fraser as "A new Agent in Ophthalmic Medicine," and in 1868 he described the now familiar "Argyll Robertson pupil."

In 1872 an event occurred, typical of the times, but which would be unusual now. The President, Mr Handyside, entertained his colleagues and the public to a conversazione in the Freemason's Hall. For this "social, scientific, and philosophical *Reunion*," as it was called, nine hundred and thirty invitations were issued and five hundred guests attended. The members outvied one another in providing scientific and medical exhibits for the interest and enjoyment of the guests. The entertainment included a collection of curios from home and foreign sources, botanical, zoological, embryological, and pathological specimens, casts, models, and drawings of all kinds, including models of the Siamese Twins and similar monstrosities, and surgical instruments and apparatus. One of the instruments shown was the stethoscope, then a comparative novelty in Edinburgh. It weighed three-quarters of a pound. The leading chemical manufacturers in Edinburgh exhibited their latest medical products. It requires little imagination to believe that the members of the Society and their guests enjoyed themselves vastly.

If one now dare venture for a moment to look ahead one is reminded of the Valedictory Address of Joseph Bell in 1894, in which he indulged in an "Outlook." He visualised a "stately hall" to embrace in an "Academy of Medicine" all the learned and scientific societies related to medicine in Edinburgh, with libraries, laboratories, and museums

and even a tea-room and a billiards room. He ended his address, however, by pointing out that the future of the Society would depend not upon premises but upon the interest and enthusiasm of its members.

Since Hamilton's time many changes have taken place in the science and practice of medicine as well as in the activities of the Society. These changes have been mainly due to advances in technology and the new knowledge which this has brought with it, and the resulting growth of specialism. The demonstration of specimens has been almost entirely supplanted by the lantern and the development of cinematography with its wonderful colour pictures, and may be expected largely to replace the exhibition of the living patient.

The old analytical chemistry, taught to medical students largely as an introduction to pharmacutics, has been outstepped by synthetic chemistry, which promises to enable us to design our remedies to produce the effects we wish, and the old polypharmacy is becoming replaced by a reasoned chemotherapy. Botany, to a great extent a legacy from the days of the herbalists, is now turned towards bacteriology and applied antibiosis forms a fitting crown to the work of Pasteur. Physics is dominated by the study and application of electricity and radioactivity in all their forms and promises to be turned in future in the direction of nuclear fission. Indeed, it is already suggested that a medical student should devote two years to the study of physics. In natural history interest is centred in parasitology and heredity. Never was there a time when medicine as a technical science seemed more pregnant with incalculable potentiality.

When present-day conditions are compared with those of a hundred years ago, the results of development in medicine become apparent. Infantile mortality is being reduced and life is being prolonged. The care of physically and mentally imperfect human beings, most of whom in Hamilton's time would not have survived, and of the aged is making an ever-increasing demand upon medical services. In future the disposal of the living, no less than the disposal of the dead, will be a major sociological and public health problem.

These and other changes make it more than ever incumbent upon us to cultivate the art of healing in addition to the science of medicine. In the future medicine of forms and regulations it will be increasingly necessary for us to remember that while the love of medicine may make medical scholars, it is the love of the patient that makes doctors.

Are we not already tending to discard the old clinical medicine and to rely more and more on machines and chemical tests in our daily work as doctors? Is there not a danger that the mechanistic side of medicine and, indeed, of life may be allowed to overshadow the humanistic side?

Our medical schools must not be allowed to develop into technical colleges: to learn how to live long is poor compensation for losing the art of living well.

The uncontrolled and inco-ordinated growth of specialism threatens to split up medicine into numerous more or less independent cults. Medicine is more than a mere summation of unrelated specialties, aggregated rather than combined, and diagnosis is more than a collection of reports. Integration is required, and the integrating factor can be supplied by no one as well as by the general practitioner, and no body of men is better fitted to pursue this object than this Society.

I would like to express my thanks to Mr Graham, Librarian of the Royal College of Physicians, for his kind help in finding details of Robert Hamilton's life.

*Dr Wilkie Millar* expressed the thanks of the Society to the President for his most interesting address. In addition, he thanked Dr Traquair on behalf of the Society for the manner in which he had filled the Presidential Chair during his term of office.

# THE INVESTIGATION OF CHRONIC DIARRHŒA IN ADULTS \*

By W. LINDSAY LAMB, M.B., F.R.C.P.E.

## DEFINITION

CHRONIC diarrhœa is a common symptom of interest to physicians and surgeons alike, though in the majority of cases it will be the physician's task to investigate the condition before treating the underlying cause. It is impossible in the time at my disposal to deal adequately with the whole subject, so I propose to confine my remarks largely to what I consider to be the important points in its investigation in adults from personal experience in hospital and private practice as well as in the Army during the recent war.

In view of the fact that every healthy individual has, what is for him, a normal bowel habit, and that this varies from person to person within fairly wide limits, it is necessary to define what I understand by diarrhœa. Thus two or three daily motions can be just as normal and compatible with perfect health as a single bowel movement every two or three days, and, provided the individual has been consistent in this respect, he can be reassured that no treatment is necessary. But the majority of healthy human beings pass a single formed stool daily, any deviation from this routine being due either to the effects of civilisation, as, for example, bad diet, laziness and overdosage with purgatives, or to some nervous or physical cause. So I define diarrhœa by calling it the abnormally frequent passage of unformed or watery stools with or without such unusual constituents in the fæces as mucus, blood or pus, the actual number varying from two or three in the day to twenty or more. Diarrhœa can be acute or chronic, but it is only with the latter that I propose to deal to-day.

## CLASSIFICATION

There are so many possible causes of chronic diarrhœa in adults that it is difficult to classify them both simply and comprehensively, but I have thought it best to err on the side of simplicity in order to be practical, even though I may not have included in my list several less common conditions which may spring to your minds.

### *Classification of Chronic Diarrhœa*

#### 1. *Functional.*

Lienteric.

Psychogenic.

Spurious—mucous colitis or mucous colic.

Gastrogenous—achlorhydria.

\* A Honyman Gillespie lecture delivered in the Royal Infirmary, 5th June 1947.

## 2. *Organic.*

### A. Known Etiology.

Toxic—drugs and poisons such as digitalis, iron and purgatives.

Hyperthyroidism, uræmia, waxy disease.

Allergic—foods.

Infective—*Salmonella* group

Chronic bacillary dysentery.

Amœbiasis.

*Bilharzia*, giardia.

Tuberculosis, syphilis.

Diverticulitis

Neoplastic—Carcinoma of colon.

Polyposis.

Deficiency diseases—Pellagra.

Chronic pancreatic disease.

Gastrocolic fistula.

### B. Uncertain Etiology.

Ulcerative colitis.

Sprue syndrome.

Regional enteritis (Crohn's Disease).

## HISTORY

As with medicine in general so in gastroenterology, I need hardly remind you that the corner-stone round which the diagnosis will be built is a well-taken history. I believe that most students and many young practitioners do not realise this sufficiently. A good history will take time, but it will not be wasted, and it should go back to the very onset of the condition, be it weeks, months or years. It should cover in chronological order any alterations in the patient's condition and general health, and I have often found it useful when the history is a long and complicated one and the patient reasonably intelligent to ask him to jot down briefly and with dates the most important landmarks. Later, and with the patient's help, these can be elaborated and elucidated. The foregoing remarks, though couched in general terms, apply with particular force to any case of longstanding diarrhœa, but there will be certain points to which special attention must be directed. I would go so far as to say that in most cases an accurate diagnosis can be arrived at from the history alone. Among the leading questions that should be put to the patient are the mode of, and age at, onset, and the total duration of his symptoms, together with enquiries as to any improvement or alternating constipation. I would stress that mere youthfulness does not of itself exclude the possibility of carcinoma of the colon, as I can recall having seen this condition in a girl of nineteen. Alternating constipation and diarrhœa is usually considered to be suggestive of a neoplasm when it occurs in

a middle-aged patient, but that it is not always so is well illustrated by the following case :—

D. C., a man of 64, was seen in the medical out-patient department some months ago because his doctor thought he might have a neoplasm of the colon. He gave a history of alternating constipation and diarrhœa of three years' duration together with some loss of weight. On examination he looked well and was not anæmic. There was nothing palpable in the abdomen or rectum, and physical examination was entirely negative. On further questioning it turned out that owing to a slight tendency to constipation he had three years ago started the habit of taking a good dose of castor oil two or three times a week. This had, of course, produced diarrhœa which, not unnaturally, was followed by constipation.

The actual time of day or night when the patient has to empty the bowel is of considerable importance. Thus it is probably safe to say that, if diarrhœa disturbs the patient at night during sleep, the cause is organic, whereas in my experience it is rare for functional diarrhœa to do so. Early morning diarrhœa is suggestive of some lesion in the rectum, such as carcinoma, or of the sprue syndrome. When it occurs immediately after a meal it may be simply due to intestinal hurry owing to an over-excitabile small bowel (lienteric), or the patient may be allergic to something in his food. For example :—

Mrs N., aged 44, was sent to the Infirmary in April 1947 on account of colicky lower abdominal pain associated with diarrhœa of two years' duration. The pain and diarrhœa occurred together and invariably came on just after a meal, especially dinner. Associated with these two symptoms was a severe itchy urticarial rash all over her body. There was no personal history of asthma but her son had this disease. Six years previously Mrs N. had been very ill with dysentery. Though the patient was unable to incriminate any particular food, the presence of urticaria, abdominal colic and diarrhœa left no reasonable doubt as to the diagnosis. Her urticaria, as well as the colic and diarrhœa, have been relieved by Anthisan. For a few days while she omitted taking Anthisan all her symptoms returned, but they immediately stopped when she started the drug once more.

Abdominal pain of any severity is much less common with chronic than acute diarrhœa and is usually referred to the lower abdomen, especially on the left side. If severe it will be colicky in character and usually due to gas in the bowel as in sprue, or associated with ulceration and spasm as in ulcerative colitis and regional enteritis. Many patients with long-standing diarrhœa, however, will complain of a constant dull ache in the left iliac fossa. It is seen in cases of organic disease such as diverticulitis, in which it is probably due to peritoneal irritation and will be associated with considerable tenderness and muscle guarding. It is also commonly present though not associated with guarding, but rather with pains elsewhere in the abdomen in cases of functional diarrhœa and especially in mucous colitis. When a man, who gives a long-standing history of epigastric pain due to a peptic ulcer, and especially if he has had a gastro-enterostomy or partial gastrectomy performed, complains of persistent



diarrhœa, it is well to keep in mind the possibility of a gastro-colic fistula, though diarrhœa following gastroenterostomy or gastrectomy is by no means uncommon even without a fistula.

Loss of weight will be a constant accompaniment of any prolonged and severe diarrhœa, and with this will go general symptoms such as tiredness and lassitude. But it is a mistake to imagine that, because a patient who has diarrhœa has not lost weight, he therefore cannot have a neoplasm in the colon. It should be our aim to diagnose these cases early and hand them over to the surgeon before they have become cachectic. It is true that, when a patient with chronic diarrhœa asserts that he has not lost weight, one is usually justified in concluding that the cause is functional, but there is no reason to suppose that psycho-neurotic patients are immune from organic diseases such as cancer. There are few more difficult problems in medicine or ones which require such a high degree of clinical acumen and judgment than that of spotting the presence of organic disease in a neurotic patient. With patience and care, however, there will be found to have been some alteration in the patient's previous symptoms. Thus a man, who for years has had diarrhœa which only occurred by day, may have to start getting up in the early morning to empty the bowel and, when he has done so, not have a feeling of complete relief, thereby focussing your attention on the possibility of a neoplasm in his rectum. Though I have mentioned this rare possibility I do not wish to over-stress it. But the opposite state of affairs is far from uncommon, in which the patient with long-standing diarrhœa of organic origin develops a superadded psychoneurosis and bowel consciousness. This was made abundantly clear to me during the war when treating large numbers of men suffering from chronic relapsing amœbic dysentery. In these cases a vicious circle was set up, and it was easy to understand how it could occur, though difficult to avoid on account of the inefficacy of the drugs in use for treating chronic amœbiasis at that time. Most patients who have passed loose motions for months or years will be able to give a fairly accurate description of their stools, and enquiries should always be made as to the presence of mucus and blood.

The first case I mentioned not long ago illustrates the importance of finding out the type and quantity of aperient the patient is in the habit of taking, and in this connection it is worth mentioning the equally pernicious habit that is frequently met with among well-to-do patients—a habit incidentally which is usually doctor-made. I refer to bowel wash-outs or colon lavage. These are the stock-in-trade for the treatment of mucous colitis at many fashionable clinics and spas both at home and abroad, though I am glad to say they do not appear to flourish north of the Border. That they have their uses I will not deny, but there is no doubt in my mind that they usually do more harm than good if only because they tend to make the patient more bowel conscious than he already is. The habit once formed is very

difficult to break, and serves to stress the importance of anxiety and worry in the ætiology of diarrhœa. One does not need to be an expert psychologist to realise the intimate connection between the two in such conditions as mucous and ulcerative colitis, and the fact that most of us have had attacks of diarrhœa under conditions of stress and strain is, to my mind, sufficient proof that anxiety may of itself be the main factor in an individual whose nervous system is unable to cope with the difficulties of his environment. The middle-aged man or woman whose whole life centres round his or her excretory functions, and who for years has kept copious notes of the number, colour and consistence of his or her motions, will be familiar to many of you. He will usually be suffering from the spurious diarrhœa of mucous colitis, which is the result of spastic constipation acquired many years before, and there will be few aperients or douches that he has not tried, thereby further insulting an already injured bowel. It is tempting to say to these patients in the words of Samuel Johnson: "Do not be like the spider, man, and spin conversation incessantly out of thine own bowels."

This, however, will not help them, and they must be treated like any other psychoneurotic by attempting to re-educate not only the bowel but the patient as a whole. Most of us find neurotic patients tiresome and a trial as indeed they often are. Yet it is probably not far from the truth to say that at least 50 per cent. of chronic illness seen in general practice is functional in origin, and that most of it is amenable to simple psychotherapy. It is a good rule not to diagnose a patient's complaint as psychogenic unless (1) physical examination and investigation are entirely negative and (2) there is positive evidence of neurosis in the patient's history and environment.

Many tropical diseases produce diarrhœa as an outstanding symptom, and it will be important in certain cases to make special enquiries about residence abroad, not forgetting that even a few days ashore at some tropical or sub-tropical port is long enough to allow entry of such organisms as *Entamæba histolytica* into the gastrointestinal tract of an unsuspecting host. Of all these diseases amœbiasis is the most likely to be common in this country for some time to come and to catch the unwary. Before the war I had not seen a single case; yet during the past year I have seen six. Its importance lies in the fact that it is usually a mild and chronic disease which, if not diagnosed and treated adequately, can have such disastrous results. The first case I ever saw, soon after arriving in Egypt, taught me a lesson I shall not forget. This man, who had only been in Egypt five weeks, was admitted to hospital with a high temperature and extensive dulness at his right base. He was thought to have pneumonia but did not respond to the sulphonamides. Though he had little if any diarrhœa, he gave a history of having had a "Gypsy Tummy" soon after landing, but as this was an almost universal complaint, little attention was paid to its true significance. In our ignorance we did

not suspect amœbiasis till it was too late. Shortly before he died he developed jaundice and a palpable tender liver, and emetine injections were begun. At autopsy eight liver abscesses were found secondary to amœbic ulcers of the cæcum. This man's life could have been saved had we had more experience of this condition and given emetine earlier.

At the risk of labouring this point, but because I think it is so important, I would like to mention another case which occurred in this hospital two years ago.

R. B., aged 43, gave a history of one year's severe diarrhœa with blood and mucus in the stool. He had been very fully investigated by a distinguished tropical expert and a diagnosis of ulcerative colitis arrived at. In fact, he had been so ill that an appendicostomy had eventually to be performed. After some time he improved sufficiently to allow him to come to Edinburgh to take up a job in September 1944. He then had no diarrhœa but was feeling very tired and depressed and was losing weight, and it was thought that there was a big psychological factor in his illness. As he was running a slight temperature he was admitted to the ward for observation, where it was found that though his stools were of normal appearance he had a leucocytosis of 12,300. He had no tenderness in the abdomen, but the liver was slightly enlarged and there were a few signs at his right base. Blood culture was negative, and it was thought that he might either have a suppurative pyelephlebitis or a subphrenic abscess secondary to his ulcerative colitis, the X-ray report being consistent with the latter. Though he had travelled extensively in Europe and the U.S.A., his nearest approach to the tropics had been Italy and Bermuda, which he had visited a good many years previously. At this stage amœbiasis was not even suspected, though it was considered likely that he had pus somewhere under his diaphragm. Some clear fluid was aspirated from the pleural cavity, but for fear of producing an empyema the needle was not pushed any further in. A surgeon who was called in thought a subphrenic abscess to be likely, but he was unwilling to explore until pus had been demonstrated. Sulphathiazole was tried without any effect and, as the patient by now was desperately ill, an attempt to get penicillin was made unsuccessfully owing to its scarcity at the time. I now quote from the notes:—"It seemed that his one and only chance was that of surgical drainage, and, as no one was willing to drain the supposed abscess unless pus had been aspirated, it was determined that an attempt to do so should be made in spite of the dangers of empyema and hæmorrhage. The worst that could happen could only hasten his end. Accordingly a large needle was inserted into the eighth intercostal space in the mid-axillary line to a depth of two and a half inches, during which time it was felt to pass through the liver. At this depth a pocket of pus was found and seven ounces aspirated before he was too weak to allow further intervention. The pus was thick and creamy, inoffensive to smell and pinkish in colour. When seen by the experts it was thought to be from an amœbic abscess of the liver, and it was decided to give a course of emetine hydrochloride by injection." From this moment he started to recover and was literally snatched from the jaws of death in the nick of time. The expert who had originally diagnosed ulcerative colitis, on being informed of this dramatic turn of events, replied, "I cannot believe for one minute the man ever had amœbic dysentery. Clinically he had acute ulcerative colitis and behaved as such. Moreover, I sigmoidoscoped him and his stools were

frequently searched for amœbæ. I could suggest that he had a liver abscess secondary to ulcerative colitis, but, on the other hand, I cannot conceive of any other hepatic abscess than an amœbic one responding so dramatically to aspiration. All I can say is that it is an absolute knock-out to me." It is easy to be wise after the event, but this man's life was undoubtedly saved by the pertinacity of the Resident in trying to find the pus, the appearance of which gave the clue to the correct diagnosis. It is always wise when there is any doubt about the presence of amœbiasis to apply the therapeutic test of giving emetine.

These, then, are a few of the more important points which have to be considered when taking the history, and I will not elaborate them further, except to say that the patient's attitude towards, and interest in, his complaint will often be of considerable help. It goes without saying that the previous and family history, including details about the social and home life, are necessary. All too often the latter are omitted though a proper understanding of them will often point to the diagnosis of some psychogenic illness.

### PHYSICAL EXAMINATION

Physical examination is a necessary sequel, though in many cases it will be quite negative. In other cases, however, the diagnosis will be clinched without much difficulty. From the simple classification I have already given you, it will be obvious that the examination must be complete and thorough, and not entirely confined to the abdomen, although, obviously, the finding of any tenderness or tumours will be most important. To illustrate this I quote another case.

A. K., a man of 31, was in July 1944 sent to the Infirmary with an eight-years' history of diarrhœa which began after a mastoid operation. He had lost two stones in weight and usually passed a pale watery stool containing undigested food after each meal. During a bad spell he would have nine to ten evacuations daily. He had sought medical advice on numerous occasions but the various remedies given were quite ineffective. He had managed to carry on with his work as a forester though he was easily tired, sweated a lot and had palpitations. On examination, though there was nothing to be made out in the abdomen, he was thin and there was a conspicuous fullness of the neck which was due to generalised enlargement of the thyroid. There was no exophthalmos or tremor, and his skin, though fairly dry, was warm. His pulse was ninety per minute. He was considered to be a case of thyrotoxicosis whose presenting symptoms was diarrhœa. This, as well as his general health, responded very satisfactorily to thiouracil plus a small dose of codein, and in six weeks his weight had gone up from eight stone three pounds to nine stone four. When last seen in November 1946 he had no diarrhœa at all and was doing a hard day's work without any difficulty.

The general state and nutrition of the patient will depend on the length and severity of the diarrhœa, being poorest in sprue and ulcerative colitis, whereas in most cases of amœbiasis and early cases of carcinoma of the colon it is remarkably good. The slowness with which some patients suffering from the latter condition lose weight

and ground has often surprised me. The presence of fever will narrow the field considerably, while even the aroma round the patient's bed can be almost diagnostic. Many of you will have noted the characteristic *faecal* smell given off by patients suffering from ulcerative colitis. The condition of the tongue, whether smooth or red, as well as the presence of anæmia and other evidence of deficiency disease, should not escape attention. Lastly, and I hesitate to mention it to this audience, in no case where diarrhœa has persisted for more than a few weeks and the cause is not certain should a rectal examination be forgotten. My excuse for reminding you about this obvious precaution is that some time ago I saw in the Medical Out-Patient Department in one morning two men past middle age, each with a history of intractable diarrhœa of some months' duration. Both had been treated unsuccessfully with various drugs, such as bismuth and kaolin, after incomplete examination. In neither case had a rectal examination been carried out, but both had palpable tumours within easy reach of the finger. I believe that the treatment of diarrhœa nowadays, whether acute or chronic, by such drugs as I have just mentioned is very seldom called for and certainly never until the cause has been found. Yet these drugs are still widely used in an indiscriminate way, and do more harm than good by giving a false sense of security and thereby avoiding the main issue, which is an accurate diagnosis. The treatment of an acute diarrhœa, which is invariably due to some infection or toxic agent, is first to find the cause and then to help Nature either by getting rid of the cause with a saline purge or castor oil, or by administering a true intestinal antiseptic of the sulphonamide group of drugs. The treatment of chronic diarrhœa is again to find the cause and treat it logically instead of packing the bowel with constipating drugs, until all else has failed. Of all palliative drugs for the treatment of chronic diarrhœa, especially when it is of functional origin, there is none more useful than Codein in half-grain doses.

### EXAMINATION OF THE STOOL

Examination of the stool by naked eye, microscopic, chemical and cultural methods will be the next step, and of these naked-eye inspection is possibly the most important yet most neglected. It is not good enough to get a report on this from a nurse or to look at a small specimen. The whole stool free from urine should be seen either in the bed-pan itself or in a large glass jar. It will then be possible to note the colour and consistence as well as the presence of mucus, blood and pus, and thus at a glance to differentiate the pseudo-diarrhœa of so-called mucous colitis in which large quantities of plain mucus or mucus casts of the bowel are present, with or without constipated lumps of *faeces* from the loose or watery stool with mucus, blood and pus of ulcerative colitis. The pale, bulky, frothy and offensive stool of typical sprue is so characteristic as to need no further

description. Unfortunately the stool of amœbiasis has no definite naked-eye appearance. It may be formed or loose, though when the disease is active it is usually loose without being watery and will contain mucus and possibly blood, though in much smaller quantities than in ulcerative colitis. The presence of mucus alone in a stool does not necessarily denote ulceration of the bowel, as it is the protective mechanism by which the large bowel reacts to the irritation of long-standing constipation or the use of aperient drugs and enemata, but the presence of mucus with blood and pus always indicates ulceration. Whenever mucus is seen by naked eye, a small piece should be placed in a drop of saline and examined microscopically for blood and pus cells, as well as for protozoal organisms of which *Entamoeba histolytica* is much the most important. These protozoa in their vegetative or active stage are so characteristic that if proper precautions are taken they can be demonstrated in the majority of, if not all, cases of active amœbiasis. They will appear as large motile structure about six to eight times larger than a pus cell, and the cytoplasm will be divided into a clear ectoplasm and a finely granular endoplasm. From the ectoplasm blunt pseudopodia, by which the amœba moves, are extruded while the endoplasm contains a fine nucleus, often hardly visible, as well as a varying number of ingested red cells. The two important points which differentiate this from *entamoeba coli* and all other amœbæ as well as from macrophage cells, and with which it may be confused, are its activity and the ingested red cells. In view of this it is important to observe some fundamental rules when a search is being made for them. They are very sensitive to the effects of both cold and antiseptics, so either the microscope must be brought to the patient or the patient sent to the laboratory. A delay of five minutes in examining the stool from the time it is passed will vitiate the whole procedure. The bed-pan, glass slide and microscope stage should be warmed and no antiseptic of any sort allowed to come in contact with the stool, which must be examined as soon as it is passed, preferably following a saline purge. With a sterile platinum loop a small piece of mucus is immediately placed in a drop of warm saline on a slide and a search for the actively motile amœbæ made forthwith. Unless mucus is present it is a waste of time to look for vegetative amœbæ though cysts may be present. But whereas the former can and should be identified with ease by the clinician, the differentiation of the cysts though theoretically quite easy by counting the number of nuclei, is not so simple a matter in practice and should be left to the tropical expert or bacteriologist. I mention these details because unless they are strictly adhered to, the number of positive stools obtained will be negligible. Microscopic examination of the stool for starch granules, muscle fibres and fatty acid crystals is said to be of assistance in deciding the state of digestion of carbohydrates, protein and fat in the diet, though in my experience this is more of theoretical interest than practical importance. The main help to be got from bacteriological

culture of the stool is in the isolation of pathological organisms of the typhoid dysentery group, though I am aware that certain experts in the past, and even nowadays, have laid great stress on the relative proportions of *B. coli* to streptococci in cases of so-called intestinal toxæmia. I do not subscribe to their views and believe that the vaccines and washouts prescribed often do more harm than good owing to the underlying psychological factor which is usually present in these cases. I need not remind you that in the majority of cases of ulcerative colitis no pathogenic organisms can be found, though at one time it was said by Hurst that these cases were the result of previous bacillary dysentery. I have certainly seen cases of this disease which gave a history of having had dysentery, especially in the 1914-1918 War, but these cases are in a very small minority. It is true that the lesions in bacillary dysentery and ulcerative colitis are indistinguishable, but the vast majority of cases of ulcerative colitis that we see in this country have never been abroad or had a proved dysentery. In my experience, chronic bacillary dysentery is now a rare condition, probably owing to modern specific therapy with sulphonamide drugs, but if it is suspected the same precautions with regard to antiseptics and early examination will have to be observed if a high percentage of positive results is desired.

The presence of red blood alone in the motion means that it is coming from low down in the bowel, and if without mucus or pus will, in most cases, be from internal hæmorrhoids or a polyp. If it persists, however, it will not be safe to assume such a simple cause, and quite apart from the fact that such bleeding over a period of time will eventually produce anæmia and all the symptoms that follow in its train, the patient should be carefully examined with a proctoscope or sigmoidoscope to exclude any more serious lesion, such as a neoplasm. The loose tarry stool of melæna due to massive bleeding high up in the gastrointestinal tract is familiar to you all, but I would like to say a few words about the benzidine test for occult blood. This is a most valuable aid to diagnosis, but it suffers from one serious drawback—it is too sensitive. For this reason, if it is not going to be misleading rather than helpful, two precautions must be observed. First, the patient must be kept on a bland meat free diet for a few days before the test; and secondly, the greatest care must be taken to see that all test tubes are scrupulously clean. On many occasions, when doing this test, I have had great difficulty with it on account of false positive results. Any small extraneous source of bleeding, as from nose or gums, will of course vitiate its correct interpretation.

The only other chemical estimation worth mention is that for fats. Though the naked eye appearance of the stool from a typical case of sprue or the mal-absorptive syndrome is so characteristic that the diagnosis from this alone is easy, in the early or larval cases as well as in the differentiation of mal-absorption from chronic pancreatic disease more accurate chemical estimation of the total as well as split and

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unsplit fats is called for. The estimation of these fats in a single specimen can be misleading, and it is advisable to carry out a proper fat balance by feeding the patient with a known quantity of fat daily, say 50 gm., and collecting the total stools passed over four to five days. In a normal individual 90 per cent. of this fat is absorbed, while anything below 85 per cent. is definitely abnormal. The normal ratio of split to unsplit fat is at least three to one, and this is usually maintained in spruce but altered in pancreatic disease.

### TEST MEAL, BLOOD EXAMINATION, ETC.

The further investigation of any case of diarrhœa will depend on the facts already disclosed, but I would remind you of a few simple clinical tests that may be helpful and are sometimes forgotten. The following case illustrates how easy this is.

J. D., a man of 69, was, in February 1947, sent into a nursing home by his doctor, under the care of a colleague to whom I am indebted for his notes about the patient. He had complained for some years of intractable diarrhœa which, two years before, had been investigated by another physician elsewhere. Physical examination and a barium enema being quite negative, he had been reassured that there was no serious organic disease. The diarrhœa, however, continued unabated in spite of various drugs, and he became pre-occupied with his bowel function to such an extent that it would have been easy to label his condition as neurotic. He had lost weight and had had repeated bouts of soreness of the tongue, for which he had been given vitamin B. Physical examination revealed nothing apart from an eczematous eruption round the anus, and both rectal examination and barium enema were once again negative. In view of his history of sore tongue, a test meal was done and he was found to have a histamine-fast achylia. He also had a high colour index anæmia with a hæmoglobin of 85 per cent., though his marrow was normoblastic. He absorbed eighty-nine per cent. of fat given by mouth. The point I wish to make, and the most dramatic feature of his case, was the complete and rapid cessation of his diarrhœa for the first time for years after he was given hydrochloric acid by mouth. When seen one month later he was having one stool daily and was feeling a new man. He had also had liver injections, though it was the acid and not the liver which controlled the diarrhœa.

This case, therefore, illustrates the importance of not forgetting the simple things in medicine amid the welter of X-rays and more elaborate tests. We all know that a test meal and a blood count are important, but the practice of medicine to-day is such a complicated business that at times we cannot see the wood for trees.

A full blood count to determine whether a patient is anæmic, and if so, the type of anæmia, as well as to determine whether there is a leucocytosis or not, especially in the presence of fever, will seldom be a waste of time, and in many cases is essential. Blood culture, agglutinations, the Frei Test and Wasserman reaction, as well as estimations of plasma proteins, serum calcium and blood urea, all

have their place which I need not elaborate. A sedimentation rate, if viewed intelligently, may be of some help in distinguishing *functional* from organic diarrhœa, but it can hardly be expected to do more than that.

### SIGMOIDOSCOPY

Sigmoidoscopy has until recently been considered to be outwith the province of all but a few physicians, and we were content to ask our surgical colleagues to do this for us. Certainly I never had done one myself before the war, or for that matter seen one done in a medical ward. But as a result of serving abroad, where it was more or less a routine part of the investigation in most cases of dysentery especially when amœbiasis was suspected, as well as experience in this country since the war, I am firmly convinced that every physician who is interested in gastroenterology should be able to pass this instrument and interpret what he sees. It is just as much an essential step in reaching a correct diagnosis where some lesion in the lower bowel is suspected, as is examination of the stool and X-ray. In many cases, indeed, it is more important than a barium enema. I recently saw a man of sixty-seven with nine months' history of diarrhœa due to carcinoma of the rectum. It was easily palpable on rectal examination, and could be seen through the sigmoidoscope, yet barium enema was quite negative. It is a simple and safe procedure which can and should be done without an anæsthetic or even an injection of morphia unless in exceptional cases. Most patients tolerate it well without much discomfort or pain, though in very nervous individuals and where there is severe ulceration of the lower rectum it may be difficult. In my opinion the best preparation for sigmoidoscopy is either nothing at all or a good dose of aperient the day before, the patient being asked to try to empty the bowel just before examination. When, however, there is severe diarrhœa with tenesmus and much mucus, blood and pus in the stool, one or more saline or alkaline bowel wash-out may be required in order to get a good view of the mucosa. In all but the most debilitated patients and possibly in nervous women, much the most satisfactory position for the patient to be in is the knee-shoulder one across the bed with the left shoulder and arm flat on the bed and the buttocks well up in the air. With the patient in the left lateral position, even when the buttocks are raised and drawn right to the edge of the bed, I have found it rather awkward and difficult owing to the examiner's head being obstructed by the patient's thighs and legs. The kind of instrument used is immaterial, though personally I prefer the older fashioned metal tube type with proximal lighting to the more modern "Cold lite" variety. The tube should be warm and well lubricated, and once the anal sphincter has been passed the obturator withdrawn. It is then pushed gently and slowly onwards under direct vision. The angle at which it is passed will vary with the direction of the bowel, and whenever the rectum has been entered

the handle of the instrument will have to be depressed considerably in order to allow the distal end to follow the curve of the sacrum until it gets near the recto-sigmoid junction. Here once again the angle is altered, as can be seen from the slide. In no circumstances should any force be used, and if any apparent obstruction is met with, a little judicious inflation of the bowel with air will show the way ahead, unless the obstruction is a real one, either from within or without the bowel. The two chief natural difficulties which have to be circumvented are firstly Houston's Valves in the rectum, though with experience they do not cause much trouble, and secondly, the recto-sigmoid junction where there is a fold of mucous membrane acting as a valve. At this point the lumen narrows and alters course and the strong pulsation of the left internal iliac artery can be seen. It is usually at this stage that the patient complains of most discomfort. After the instrument has reached a point between 22-28 cm. from the anus, it should be slowly withdrawn and the mucosa thoroughly inspected in so doing. The normal mucous membrane is of a uniformly pale pinkish colour with the thin vessels clearly visible branching in all directions. When healthy it does not bleed unless it is severely traumatised, but when hyperæmic and ulcerated it will bleed easily. Ulcers will vary in size, shape and number as well as in situation according to the severity and cause of the condition. Those of bacillary dysentery and ulcerative colitis are identical and are superficial, covering large areas of the mucous surface. They have ragged edges and are serpiginous in outline, the intervening mucous membrane being unhealthy and hyperæmia. In severe cases no healthy mucosa is visible throughout the rectum which is the part of the bowel most frequently and severely involved. In contrast to this the ulcers of chronic amœbic dysentery are deep and extend into the sub-mucosa so that they appear in the early stages as small heaped-up spots of pus rather rounded or oval in outline and varying in size but rarely very large. They are circumscribed and discrete and, though there may be a surrounding zone of hyperæmia, the intervening mucous membrane appears perfectly healthy. Later the pus bursts into the lumen of the bowel and produces a deep ulcer with undermined edges and necrotic base. The ulcers will vary in number from one or two, which may easily be missed in a mild case, to several dozen. They are commonly seen on the mucosal folds of the rectum and especially on the free edges of Houston's Valves. Whenever ulcers are seen, a scraping with a long-handled spoon should be taken for immediate microscopic examination and culture. Soon after a full course of treatment these amœbic ulcers will have disappeared and the mucous membrane will have a pitted or granular appearance. Of course, a negative finding in the rectum does not exclude amœbiasis as lesions may be present anywhere in the colon, though the cæcum and rectum are the commonest sites involved. The appearances of an ulcerating neoplasm of the lower bowel are so characteristic that I need not describe them to you,

though sometimes mistakes can be made, as the following case illustrates :—

Mrs A. A., aged 41, was seen in the Medical Out-Patient Department in December 1945. She gave a history of gradual onset of diarrhoea with mucus and blood but no fever since February 1945. She had not lost much weight and had managed to carry on with her housework in spite of some tiredness. Physical as well as rectal examination was negative, and I came to the provisional diagnosis of ulcerative colitis or a neoplasm. She was admitted to the ward in January 1946, and again examination was negative, but the stool contained mucus, blood and pus. On sigmoidoscopic examination there appeared to be high-up, just beyond the rectum, an angry red-looking mass umbilicated in the centre, from which a muco-purulent discharge was coming. The rest of the bowel appeared normal. I decided that she had a neoplasm, and on the strength of this asked a surgeon to see her. Without further sigmoidoscopy he opened the abdomen, but instead of a neoplasm found a small segment of pelvic colon three to four inches long which was intensely congested and œdematous and sharply demarcated from healthy bowel above and below. There were numerous apparently inflammatory glands in the meso-colon. No other lesion was seen and the abdomen was closed, a provisional diagnosis of regional enteritis or colitis being made even though a single segment of large bowel was solely involved. What I had taken to be a tumour must have been the lower end of this segment. The later history of this woman is interesting if a bit confusing. She reported from time to time and appeared to keep well, though the motions continued to be loose and to contain mucus but no blood or pus. She put on one stone in weight. In August 1946, however, she developed a chill which was followed by fever and a return of diarrhoea with blood in the stools and she was readmitted to the ward. She was treated with succinyl sulphathiazole and seemed to be improving, when the abdomen became very distended and peristalsis was visible. There was now no bowel movement, apart from pus which was collecting in the rectum. As she had no pain and little rise in pulse rate, it was decided to treat her conservatively, though she had obviously obstructed, at least partially. After being very ill for two weeks her symptoms settled down and her bowels became satisfactory once again. We considered that our diagnosis of Crohn's disease had been strengthened. But on sigmoidoscopic examination the appearances were now in keeping with those of ulcerative colitis. She left hospital in November 1946 much better. In April 1947 she reported again feeling very well. She had put on seven pounds in weight and was passing two stools daily—one formed one first thing in the morning and another looser one with some mucus soon after. On physical examination there appeared to be slight fullness over the right iliac fossa, and I thought the cæcal region was somewhat thickened. The specimen of stool she brought with her was quite formed and normal. Sigmoidoscopic examination on 7.5.47 now showed a much more healthy mucous membrane. There were some areas of hyperæmia, and low down in the rectum the mucosa appeared rather granular, but there were no ulcers. She was sent for a barium follow-through and enema which showed narrowing of the lumen of the rectum, sigmoid and descending colon associated with some spasm. The rest of the colon and terminal ileum filled normally, so it would seem that the final diagnosis must be ulcerative colitis, though after seeing this patient I have often wondered whether there may not be some connection between ulcerative colitis and regional enteritis..

Before leaving the subject of sigmoidoscopy, I should like to mention polyposis of the colon. During the past year I have seen in hospital two men aged twenty-two and forty who complained of mild but persistent diarrhœa. Both had served in India where they had had some diarrhœa, in each case said to have been amœbic in origin. When admitted to hospital, however, no amœbæ were found in the stools in either case. On sigmoidoscopic examination the man of twenty-two had a single large smooth tumour about the size of a marble fairly low down in the rectum, while in the older man there were multiple small polypoid looking tumours in both rectum and pelvic colon. I considered it advisable in each case to give a full course of anti-amœbic treatment in view of the possibility of the tumours being amœbomata. There was, however, no change after treatment, and both were referred to a surgeon who suggested barium enema and biopsy, as he considered they might have a generalised polyposis. In the young man of twenty-two, enema showed some spasticity of the descending colon, and the cæcum also showed evidence of colitis, both of which were in keeping with a previous amœbic dysentery, but there was nothing else. Biopsy then revealed that the large polyp in his rectum was an adenomatous papilloma showing cystic degeneration, and it was thought to be secondary to dysenteric ulceration. As the condition was so localised, nothing further was done, beyond removing the polyp. On the other hand, barium enema in the older man with the multiple small polyps in his rectum showed that the condition was widespread throughout the transverse and descending colon as well. In fact, he was suffering from multiple polyposis in which the outlook is very serious, owing to the fact that 100 per cent. of cases eventually undergo malignant degeneration. He was, therefore, recommended to have a complete colectomy, and has already had an ileostomy which is the first stage of this formidable operation. It is remarkable how well patients get on after this operation and what normal lives they can lead. The importance, therefore, of early diagnosis and operation in these cases is obvious and depends largely on the sigmoidoscope.

These, then, are some of the commoner conditions that are seen through the sigmoidoscope. That there are others equally important I am well aware, but I have neither the time nor the personal experience to deal with them adequately. I hope, however, I have said enough to convince you of the importance of this instrument in the diagnosis of intestinal diseases.

### X-RAYS

The final step in the investigation will be an X-ray following a barium enema, and in some cases a barium meal and follow-through. The enema will demonstrate the anatomy and morphology of the large bowel as well as lesions between the rectum and cæcum, especially those which are out of reach of the examining finger or sigmoidoscope.

But it is a serious error to imagine that it can take the place of either. It is also the method of choice for demonstrating a gastrocolic fistula in which chronic diarrhoea with pale fatty stools and other symptoms of the malabsorptive or sprue syndrome are characteristic features. Contrary to what you might expect, such a fistula is more commonly seen on an X-ray plate following an enema than a meal, because the opening is usually so small and more pressure can be exerted on the column of barium from below than above. In addition to gastrocolic fistula, some of the pathological causes of chronic diarrhoea which have characteristic appearances after barium enema are diverticulitis, neoplasm, multiple polyposis and ulcerative colitis. The differentiation of diverticulitis and carcinoma of the sigmoid colon, however, both clinically and radiologically and even at operation, is sometimes no easy matter. It is important to remember that, when a carcinoma or other obstructive lesion in the colon is suspected, a barium enema is to be preferred to a meal as the latter may precipitate a complete obstruction in virtue of the barium becoming solid. In contrast to the well-known appearances of the colon both in health and disease following a barium enema, it is surprising how little is known about the small intestine as demonstrated by X-rays after a barium follow-through. I refer, of course, to the jejunum and ileum in disorders of which diarrhoea is a prominent symptom. To those of you who are interested in this subject, I would commend a monograph by Ross Golden (1945). Such a follow-through, when properly done, is a time-consuming business, but it is of help in understanding the normal physiology of as well as abnormal states affecting the small intestine. The normal feathery appearance of the jejunum and the smoother tube-like outline of the ileum will be familiar to you all as will the gross structural changes associated with regional enteritis. Golden, however, draws attention to what has sometimes been described as the "Deficiency Pattern," but which he prefers to call "Disordered Motor Function" of the small intestine in which the motility and mucosal pattern show characteristic changes. These changes are not pathognomonic or in any way specific and vary with the severity of the condition, but occur in a group of nutritional disorders in which the digestion and absorption of food substances is interfered with. These disorders are either primary, such as sprue, coeliac disease, and certain vitamin deficiency states, especially of the B complex; or secondary to some other disease, such as peptic ulcer, carcinoma, and diseases of the small intestine such as tuberculosis. In fact hypoproteinaemia from whatever cause will produce these changes, which are probably due to submucosal oedema and degenerative changes in Auerbach's plexus. The importance of their early recognition lies in the fact that they may call attention to certain unsuspected possibilities, the treatment of which will prevent the deficiency state with all its complications from developing further.

Sometimes fatty stools with other signs of malabsorption are caused

by blockage of the lacteals by enlarged abdominal glands, especially due to tuberculous infection. I have seen two such cases within the last year. A flat X-ray of the abdomen, therefore, may be helpful in showing up calcified abdominal glands, though in my experience of these cases the glands are rarely calcified, and more help in arriving at an accurate diagnosis is got from the history and feel of the abdomen. Apart from demonstrating an active tuberculous focus in the lungs of which secondary ulceration of the bowel causing diarrhœa is a common complication, an X-ray of the chest is essential in cases of amœbic dysentery, especially when hepatitis is suspected. Both screen examination and an X-ray plate of the diaphragmatic region are desirable in order to show the presence of diminished movement or upward displacement of the right leaf of the diaphragm. I have frequently seen the liver enlarge upwards in this condition without any corresponding increase downwards.

Should a liver abscess be suspected, careful and thorough exploration with a wide bore needle, preferably after one or two injections of emetine have been given to the patient, is essential. As with any collection of pus in any part of the body, it is better to be safe than sorry and to explore with a needle during life and find nothing than to let the patient die without attempting this simple operation only to find the abscess post-mortem.

In conclusion I hope I have said enough to make it clear that chronic diarrhœa is a symptom in assessing the cause of which there should be no short cut. Sometimes it is easy, but it is probably true to say that more mistakes are made through forgetting the simple things such as a complete physical and rectal examination than by omitting more complicated biochemical estimations and X-rays.

In the Gospel according to St Mark, Chapter v, Verses 25 and 26, we read :—

“And a certain woman which had an issue of blood twelve years, and had suffered many things of many physicians and had spent all that she had, and was nothing bettered, but rather grew worse.”

Which of us can deny that even to-day these words have some truth, though there should be little excuse for them ?

Many of the patients I have discussed have been in Professor Dunlop's Ward, and I would like to thank him in particular for allowing me to quote their cases and for his unfailing help. Mr Paterson Brown, Mr Quarry Wood, Dr Ian Hill, Dr Donald and Dr Hunter are other colleagues to whom I am grateful for their co-operation, as well as Sister Anderson in Ward 22. I am indebted to Professor Learmonth for the loan of the slides of sigmoidoscopic appearances and to Dr Shearer for the slides of X-rays.

#### REFERENCE

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## SCOTTISH PIONEERS IN TROPICAL MEDICINE \*

By Sir PHILIP MANSON-BAHR, C.M.G., D.S.O.

President of the Royal Society of Tropical Medicine and Hygiene

"Lives of great men all remind us  
We can make our lives sublime  
And departing leave behind us  
Footprints on the sands of time."

IT would be presumptuous for any but a medical historian to put before you a record, however incomplete, of the achievements of Scottish pioneers in general, even in such a restricted field as the subject of my lecture to-night, so I shall confine myself to a story laying emphasis on those past masters with whom I have had the pleasure of personal acquaintance during the last forty years. Having no claims to your blood, I can at least boast that I am Scotch by upbringing, because a little of your culture was inculcated by my Scots nurse, who, I need hardly add, was a remarkable woman, and her name was Marion Robertson.

Whilst just escaped from apron-strings and before embarking upon medical studies, I had been an ardent explorer of your Highlands and had been attracted by their scenery and wild life, so as a field-naturalist, armed with sketch book, field glasses and camera, I had roamed your hills, your moors and "braes around" in company with such distinguished Scotch ornithologists as Harvie Brown and Eagle Clarke, to whom I owe the boon of long friendship, and now, as years have rolled by, I can review the past and discern your misty blue mountains, the haunt of the dotterel, ptarmigan and snow-bunting, in the dim background, the moors, burns and lochs in the middle distance, whilst in the foreground there nestles enshrined within its circle of hills, like some ancient eyrie, this great city of Edinburgh, whence have flown many lusty eaglets to the four quarters of the globe, bearing with them the torch of knowledge, and returning after many days with their quarry in their talons to found this northern school of tropical medicine and to foster this branch of our Royal Society.

In the *dim misty background* of history my saga of tropical medicine commences over two hundred years ago with *James Lind* (1716-1794), the man of destiny and pioneer of vitamin deficiency. He was a native of Edinburgh and at the same time a graduate of its University. His *Essay on Diseases Incidental to Europeans in Hot Climates* (1768) may well be regarded as the first manual on tropical diseases. At the age of twenty-three he joined the Naval Medical Service and spent the next ten years at sea, mainly in the tropics.

\* Delivered to the Edinburgh Branch of the Royal Society of Tropical Medicine.

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References: Shortage of space precludes list of references, but full documentation may be obtained on application to Clinical Research Dept. 35. J.



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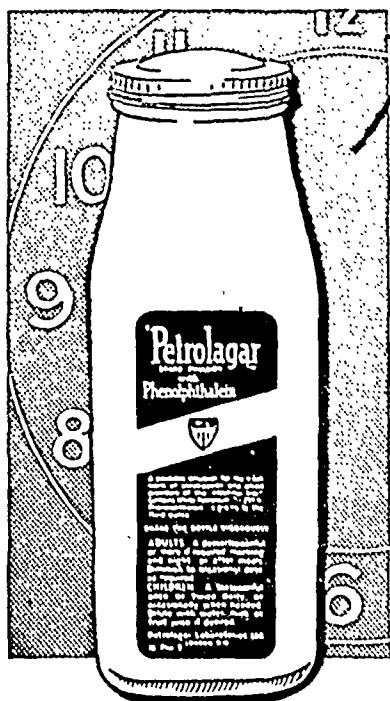
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The conditions under which seamen lived were, of course, just indescribably bad, and on long voyages they were particularly liable to scurvy. Returning to Edinburgh he published in 1753 his *Treatise on Scurvy*, a work which forms a landmark in medicine and attracted general attention. Eventually, in 1794, the year in which he died, an order was issued for a ration of lemon juice to be supplied to a squadron sailing to the East Indies. This was entirely successful and formed the starting point of the abolition of this scourge from ships at sea and the basis of our knowledge of the vitamins.

Lind was a clear thinker, an acute observer and a good clinician—a wondrous combination. His name is to be numbered amongst the great when he wrote: "For the number of seamen in time of war who die by shipwreck, capture, famine, fire and sword are not inconsiderable in respect of such as are destroyed by ship diseases and by the usual maladies of intemperate climates."

To *James Grainger* (1721-1766) we owe much. He was born in Berwickshire and graduated in Edinburgh in 1753. After a period as an army surgeon and a time in practice in London, he set sail for St Kitts in the West Indies in 1759, and some five years later (1764) wrote an *Essay on the More Common West Indian Diseases and the Remedies which that Country Produces*, to which were added "some hints on the management of the negroes." He had had the advantage of having been a friend of Samuel Johnson in London and of having devoted some time to poetry. In his book he expresses views well in advance of his day and with extraordinary perspicuity distinguished between two types of dysentery: one curable by ipecacuanha and one not. He further advocated "sick houses" or estate hospitals, and for the first time put forward the provision of isolation and venereal wards.

A more important writer upon the diseases of the West Indies, but one whose name is not so well known, was *William Wright* (1735-1819). He served as an apprentice at Falkirk, made a voyage to Greenland and then joined the Naval Medical Service. This does not sound exactly tropical, but he soon left the Navy and settled in Jamaica, where he had ample opportunities of studying the diseases of that island. Returning to England he became a regimental surgeon, and being captured by the French he was a prisoner of war for some time in Spain, where he practised his medicine upon the Spaniards. He went again to Jamaica, and returning to England was put in charge of military hospitals in Barbadoes where he died.

A prolific writer and lecturer, he was elected a fellow of the Royal Society. Amongst others was his discovery of *Cinchona jamaicensis* which he believed to be three times as powerful as the bark of *C. officinalis* in the treatment of malaria. He also wrote a description of yaws which he differentiated from syphilis. His book on *Practical Observations on the Treatment of Acute Diseases in the West Indies* still forms a valuable record.

We may next discern *David Livingstone* (1813-1873) who is better known as a great explorer than as a medical man, but in many ways he remains one of the great pioneers of tropical medicine. He was a distinguished student of the Glasgow School, and it is of some interest to call to mind that the name of Livingstone figures in the forebears of Patrick Manson who became his counterpart in other directions.

Leaving Scotland for West Africa in 1840 he spent the next thirty years constantly engaged in missionary work and exploration. He was one of the earliest practitioners (1842) to make systematic clinical observations with the thermometer. He was also an advocate of the wet pack and a staunch believer in the virtues of quinine, and he seems in some way to have associated the tsetse fly with negro lethargy, or sleeping sickness.

In *Charles Morchead* (1807-1882) we have an example of a good doctor. He studied medicine in Edinburgh and Paris before joining the Bombay Medical Service in 1829. His fame rests on his book, *Researches upon the Diseases of India* (1856). He was perfectly correct in railing against the use of mercury in tropical diseases. A pioneer of medical education in India, he had the added advantage of being a skilled draughtsman.

*George Bidie* (1830-1913), of stern and handsome mien, was the prototype of the militant medical. He was born an Edinburgh native, graduating in 1853. He served through the Indian Mutiny and was possessed of an encyclopædic knowledge, for he was an authority on natural history, botany, economic products and even on coinage. He investigated the borer insect of coffee estates by which he did great service to the planters. In medicine his work on cholera and contagion by water was most important. He also introduced the humane treatment of the insane to India.

The name of *Sir John Kirk* (1836-1922) should be mentioned in the same breath as that of Livingstone. He was born in Ayrshire, graduating in Edinburgh in 1856. As in so many of our pioneers, he early distinguished himself in natural history and botany. After serving in the Crimean War, he became consul at Zanzibar where, owing to his influence with the Sultan, he did so much to suppress the slave trade in East Africa, and in doing so furthered exploration in this part of the world.

*The middle distance* of our canvas is lit up with shafts of brilliant sunshine filtering through the clouds. This period of fifty years can be regarded as the Golden Age of Tropical Medicine—an age of positive achievement. It commences with *Thomas Spencer Cobbold* (1828-1886), a man who was the Leiper of his day and did much to further parasitology and who had intimate contacts with Manson. He graduated M.D. Edinburgh in 1851 and was indeed a pioneer, and though very much a stay-at-home, his name must be included with the very great, because he classified and named many of the important tropical parasites. Manson always had recourse to him in his early

days in Amoy, China. He was therefore a great supporter of his and presided over the historic meeting in London which discussed Manson's epoch-making paper in 1879 on the transmission of the filaria (*F. bancrofti*) through the mosquito. In 1939 an ancient bent old man with a skull cap came to the London School and explained that he was the sole survivor of that meeting. He said "some thought that it was the work of a genius, but others that it was the delirious emanations from the brain of a drunken Scotsman in far-off China."

Cobbold's best-known work was a *Manual of Reference to all the Known Species of Entozoa and Ectozoa which are found Infesting Man* (1882).

The first lecturer on tropical diseases at Edinburgh—*A. W. P. Pinkerton* (1829-1861)—deserves some mention, although his memory appears to have been forgotten till it was revived by Colonel E. D. W. Greig in 1940. He was born at Dollar, studied medicine in Edinburgh and served in the Crimea where he was attached to the 72nd Highlanders. He next saw service in India during the Mutiny and later still contracted cholera; therefore it was very natural that he should be interested in this disease and that he should write extensively upon it. In 1861 he served in Aden and there he died of a fever. He is described as "tall of stature, gentle in manner, kindly in disposition, so that he was equally beloved by his friends in civil life and dear to his comrades in camp. He knew no one who did not become his friend, and by no friend will he ever be forgotten." He commenced to lecture on tropical diseases in the extra-academical school in Edinburgh in 1857, and it is clear that the Medical School of this University can claim the honour and credit of having been the first in the country, or indeed elsewhere, to produce a lecturer on the special subject of Diseases of Tropical Climates (Greig, E. D. W. (1940), *Journ. Trop. Med.*, p. 77).

Dobell wrote of *Timothy Richard Lewis* (1841-1886) that he should be known as the "Godfather of Tropical Medicine," and although he was a Welshman, he must be included because he lost his nationality by virtue of his Scotch education, graduating at Aberdeen in 1867. Straightaway he entered the Army Medical Service, and in India pursued lines of research at the instigation of Cobbold. He was a very distinguished man who became a Fellow of the Royal Society for his discoveries in tropical medicine. Amongst others he gave the first authentic account of the amœbæ in the human intestine. He it was who discovered the *Filaria sanguinis hominis* in the blood of natives of Calcutta in 1872 and traced its connection with chyluria. At the time of Manson's work on mosquito transmission he was in correspondence with him (1878) and made some pertinent criticisms. In the same year he published his famous memoir on *The Microscopic Organisms Found in the Blood of Man and Animals and their Relation to Diseases*. Therein he described the trypanosome of the rat which now bears his name.

The name of *David Douglas Cunningham* (1843-1914) must be linked with that of Lewis, because he was a friend and colleague, and, in this capacity, shared many of his scientific triumphs with him and he was almost, if not quite, as distinguished; he also obtained the Fellowship of the Royal Society. He was a typical Scot, with his friendly face and his friendly dog. His features, disposition and character were also of this city of Edinburgh. He owed a great deal to his school days on the Firth of Forth, where he received a naturalist's training and where the harvest of the sea exercised its fascination over him. He also joined the Bombay Medical Service, and to him fell the honour of describing for the first time and accurately *Entamoeba coli*, *Trichomonas intestinalis* and also *Chilomastix mesnili*, and, even more important still, bodies in oriental sore which he distinguished under the name of "sporoid bodies" in 1885. He therefore has undoubtedly priority over the Russian, Borovsky, who found these bodies in 1898 in Tashkent (Hoare). He was a pioneer, too, in the manufacture of quinine and must be accounted an able, accurate and sound scientist. He was also the first to describe the fluke *Cladorchis watsoni*.

This fruitful period was graced also by *Andrew Davidson* (1836-1918), who studied medicine in Edinburgh and began his tropical career as resident medical officer to the Court in Madagascar. A most distinguished son of his University, his name has been in imminent danger of having nearly been forgotten. In 1877 he found his way to Mauritius where he had an extensive experience in malaria. He was a linguist of note and even wrote a book on the medical diseases of Madagascar in Malagassy. As a man of very considerable ability he was appointed lecturer on tropical diseases at Edinburgh University, and was the author of two standard works, *Geographical Pathology* and *Hygiene and Diseases of Warm Climates*; the latter continued for many years as a textbook for students in Great Britain and abroad and came to be regarded as the precursor to Manson's *Tropical Diseases*. I can claim some connection with this good and great man, for his son, Colonel Davidson, A.M.S., was the A.D.M.S. of the 51st Division with which I served during the first year of the 1914-1918 war, and to him, I now know, I owe my seconding to Gallipoli and Egypt in 1915 to work on dysentery and which proved indeed to be a milestone in my own career.

Amongst pioneers we must include administrators as well as research workers. *Sir William MacGregor* (1846-1919) was one such. He was a true proconsul and rose to a high position in the State where, by his wise appreciation of the importance of tropical medicine, he did much to advance our science. The son of a farm labourer, he was born at Fowie, Aberdeenshire. Mainly by his own efforts and assisted by friends he graduated at Aberdeen. In 1874 he became Chief Medical Officer in Fiji, soon after its occupation by the Crown, and under King Thakembau. Soon after he transferred to

administration and became successively Governor of British New Guinea, Nigeria, Newfoundland, and eventually of Queensland. Had he not been a great governor he would assuredly have been a great doctor. Every night, it is said, he read from his Greek Testament, and he was also well versed in French and Italian. He was also a mathematician, a practised surveyor, a lapidary and indeed a master in many arts. He was a genuine sincere administrator and one who appreciated the value of sanitation in colonial development.

Of *Sir Patrick Manson* (1844-1922) I cannot well say more than what I have already written in his *Life* (1927) and in other communications about his career. He was indeed the greatest of the pioneers, and deserved the title of the "Father of Modern Tropical Medicine" bestowed upon him by Blanchard. Others see in his life the commencement of the real era of scientific tropical medicine, as one who clarified the issue and as one who, once and for all, established the truth of insect-borne disease. It was he who provided a rallying-post for other pioneers, and he had links with them all, with Balfour, with Leiper, with Leishman, Carmichael Low, Simpson, and others who are the subject of discourse to-night, and I have shown that his influence radiated even into the past as far back as the days of Livingstone. Many have supposed that, owing to his name, Manson was an Irishman, and the Irish themselves have connected him in some nebulous manner with their patron saint. On the contrary, he was a Scot of the Scots, being born and raised in Old Meldrum, Aberdeenshire, and when he spoke his speech was, on occasions, well flavoured with Doric salt. Educated at Marischal College, Aberdeen, he remained until his death a true loyal son of that great University. We think of him here to-night as one of the founders of this Society and as its first President in 1907. Posterity will undoubtedly regard as the greatest of all his works the foundation of the London School of Tropical Medicine in 1899. As an investigator, clinician, teacher and organiser he was of first rank, and posterity will, no doubt, allot him his due place amongst the great. His links with Edinburgh were many. He studied at different times in its University and had many friends in this city. A lifelong association was with Richard Muir, surely the greatest technician of his time, and the one who prepared those admirable microphotographs which illustrated the first edition of his famous *Tropical Diseases*.

Tropical hygiene as a subject had been much neglected till the advent of *Sir William John Ritchie Simpson* (1855-1931) who, like Manson, was educated at Aberdeen, graduating in 1876. After a period as health officer in his native city, he moved to London and studied at King's College. Devoting himself to public health he became health officer for Calcutta in 1886 and remained there for eleven years. During that time he had a good general experience of tropical diseases and became an authority on plague. When Manson was organising the London School of Tropical Medicine, he joined



the staff as the lecturer on tropical hygiene. Indeed, he may justly be regarded as the first exponent of this important subject in this country, and in that capacity served on many Government committees. Therefore from time to time he went abroad on various Government enquiries, such as that of plague in Hong Kong in 1902, and of the sanitary conditions of Singapore in 1906. He made other journeys to West Africa in 1908 and 1924 and was in East Africa from 1913-1919. In 1916 he published his important text-book on *The Maintenance of Health in the Tropics*. On entering the Tropical School in 1909 I attended his lectures. They were certainly good as far as the standards of those days went, but he had a hesitating speech and a halting manner and, though he was a sincere apostle of the goddess Hygeia, I concluded that he did not arouse the same fervour in my breast. Simpson was President of this Society from 1909 to 1921.

A master of great achievement and whose name is a household word was *Sir William Boog Leishman* (1865-1926), who was by birth and upbringing a Glaswegian. The son of the Professor of Midwifery in that city, medicine and science, so to speak, were bred in the bone. Joining the Army Medical Service he spent seven years in India (1890-1897) and served in the Warizistan campaign from 1894-1895. Becoming Professor of Pathology at Netley in 1899 he occupied that post until 1913, and there, in 1901, produced the stain which bears his name, an achievement which has withstood the test of time. It was there, too, that he came into contact with Sir Almroth Wright and became interested in the bacteriology of typhoid which had worked such havoc in the South African War. In conjunction with him he perfected the technique of anti-typhoid inoculation, the triumph of which was proved in the first world war. Possibly, however, he is best known for his discovery with Colonel Donovan in 1903 of the parasite which now bears the name of *Leishmania*. He became a Fellow of the Royal Society in 1910. He was a great friend and admirer of Sir Patrick Manson. I knew him well after I came into contact with him from 1918 onwards. He was charming, courteous and most encouraging to younger men, the direct antithesis of the stiff-necked bureaucrat a D.G. of the Army Medical Service is popularly supposed to be. He was President of this Society from 1911-1913.

In *Sir James Cantlie* (1851-1926) we recognise the first example of a tropical surgeon who, at the same time, might well be described as the Harry Lauder of tropical medicine. A Highlander he was born and a Highlander he died. He was gay, witty and possessed a streak of Robby Burns coursing through his veins. A lifelong friend and associate of Patrick Manson, they were indeed a David and Jonathan to one another, for Cantlie migrated to Hong Kong in 1887 and was intimately connected with Manson in practice there. Educated in Aberdeen he graduated there in 1873. For some years he was demonstrator of anatomy and assistant surgeon at Charing Cross Hospital. Indeed, as Manson was wont to remark, Cantlie was by

instinct a great anatomist and a unique demonstrator of his subject, one who would undoubtedly have made his mark in anatomy. It has been said that Cantlie did not contribute towards the scientific side of medicine, but this is by no means true, because by his demonstration of compensatory hypertrophy of the left hepatic lobe following the destruction of the right (1898), he laid the foundation of the correct anatomical division of the liver and the deflection of the two streams in the portal circulation in what is known as the bilaterality of the liver. In 1898 he founded the *Journal of Tropical Medicine*, and in 1907 he was the instigator of this Society which has continued to flourish ever since, and from 1921-1923 he was its President. Amongst other contributions was his method of draining liver abscess by his own trocar (Cantlie's trocar), and his insistence on the treatment of sprue by a diet of meat in complete disregard of the milk treatment which had made his friend and colleague—Patrick Manson—famous. He was thus the first exponent of the high protein dietary. Returning from Hong Kong to join Manson as lecturer on tropical surgery to the London School, and as Surgeon to the Seamen's Hospital Society, he found himself in demand as a public speaker, being possessed of native wit and considerable poetic talent. Who can ever forget the famous tribute to Bagshawe on his return from a sleeping-sickness expedition to Uganda?—

" His heart's in Uganda a-chasing the Fly  
The trypanosome trembles when Bagshawe is nigh."

I had many dealings with Cantlie and found him the kindest and most considerate of souls, and we should all rejoice at the success of his fine sons in their respective careers. Especially would he have been proud of the elevation of Major-General Neil Cantlie to be the next D.G. of the Army Medical Service.

An entirely different character was *Sir Andrew Balfour* (1873-1931) who was the embodiment of the *ingenuum perfervidum scotorum*, and who still lives with us in spirit, for of all men he was an ardent biographer of the pioneers and wrote extensively and most entertainingly about them in his Presidential Address (*Trans. Roy. Soc. Trop. Med. & Hyg.* (1925), 19, 189-229). His motto was from Walt Whitman :—

" On and on in compact ranks,  
With accessions ever waiting, we must never yield or falter,  
Through the battle, through defeat, moving yet and never stopping.  
Pioneers ! O Pioneers ! "

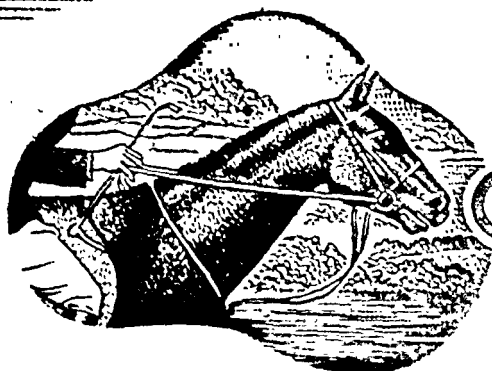
Balfour in person and appearance exemplified to a remarkable degree the best qualities of his race and of the City of Edinburgh to which he belonged. Not only was he the son of this city, but also of its soil, because he sprang from a well-known family and his father was a much-beloved and respected physician. Andrew Balfour has been described as a "rock of a man." He was honest, sincere and incredibly industrious. In addition to academic distinctions he was an all-round

athlete, being famed especially in Rugby football. He was a bustling, dribbling forward of the winger type, always prominent in the maul. After playing for Edinburgh and Cambridge Universities, he eventually gained his cap for Scotland. It may be said from that time onwards his soul dwelt at Murrayfield, so that in after life he was at a loss at which altar to worship most, that of Hygeia or that of Vulcan. He was a novelist, too, of some note and wrote at least one good novel—*The Golden Kingdom* (1903). As Medical Officer to Khartoum from 1902-1913, his cognomen was elevated from that of "Beefy Balfour" of his student days to the much more high-sounding title of "Balfour of Khartoum." He did much for the capital of the Sudan. He swept away the filthy hovels of the Khalifa; he banished malaria; he cleaned the streets and converted the Augean stables of the Mahdi into the modern well-sanitated city of Khartoum. He served with distinction in South Africa, 1899-1901, and during the 1914-1918 War he was on a roving commission which became known as "Balfour's Circus." It was then that I came into contact with him. I was fired with his imagination, his sincerity and enthusiasm, and this friendship lasted until his untimely death in 1931. In 1923 he became director of the London School of Hygiene and Tropical Medicine, and for the next eight years he was subjected to great strain in organising every detail of this great enterprise and in directing its studies, until he broke down under the burden. In his early days in Khartoum he did some first-class work on the morphology of the blood cells and on the transmission of spirochaetes through ticks in which he postulated a granular phase of what were known as "Balfour's bodies." Although he may not have been responsible for any major discovery, yet he has many claims to the rank of pioneer, because of his devotion to the cause and for the industrious, painstaking review of current literature for which he undertook personal responsibility and which eventually became the bed-rock on which the Bureau of Hygiene and Tropical Diseases was founded. He was the originator of many alliterations, of which the "filthy feet of faecal feeding flies" is the best known. I sang of him on the festive occasion of his knighthood—

" As now within this wondrous House  
All creeds and faiths united  
Mosquito, tryp, fly, fluke and louse  
Salute A. B., the knighted."

Andrew Balfour was President of this Society from 1925 to 1927. Amongst many other accomplishments he was a good actor. It is related that as a student he disguised himself as an old woman and had the audacity to consult his own father, who failed to recognise him. The malady—some cardiac disturbance—being duly diagnosed he paid his fee, but luckily for the success of his venture he was not forced to undress!!

It is with some hesitation that I include *Alfred William Alcock* (1859-1933), but I do so because he is so intimately linked with other



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*dramatis personæ*. He was the first Professor of Medical Zoology in the University of London, and provides us with another example of an Englishman who was converted to Scottish ideals by virtue of his medical education which he received in Aberdeen. Alcock was born in Bombay and was at first apprenticed to the coffee-planting industry in South India, but this proved distasteful to him, though at least it taught him to be a good naturalist and to take an interest in crustacea, of which group he rose to be an authority, and it was for his systematic work on these creatures that he was made a Fellow of the Royal Society in 1901. After trying his hand at school mastering, by his own force of conviction and aided by kind friends he came to Scotland and matriculated in 1881 and took his medical degree in 1885. It was in Aberdeen that he attended the lectures of Sir Alexander Ogston and learned from his lips the wonderful story of Manson's discoveries in filariasis in far-off China. That awoke a fire in his breast which was never extinguished. He returned to India in 1886 and eventually joined the Indian Marine Survey as Surgeon-Naturalist on board R.I.M.S. "Investigator," in which he scoured the Indian Seas. His experiences of three happy years he epitomised in a fascinating book, *A Naturalist in Indian Seas* (1902). Alcock was one of those rare phenomena, a man of science with a classical background. He was well read in the classics, literature and poetry. To him Homer, Cicero, Plato and Ovid were open books and there seldom was issued a review or article in his name which was not embellished by some classical allusion. He returned to England to join the London School of Tropical Medicine as Medical Entomologist. "Manson," he wrote, "was the magnet that drew me. I have held the faith and now I have finished my course." Alcock established the entomological department at the School; he organised and amplified the collections. For the use of students he compiled that popular book, *Entomology for Medical Officers*. In 1927 he collaborated with me in writing the *Life and Work of Sir Patrick Manson* whose career and character he so much desired. His life, like that of old Pittacus of Mitylene, whom he loved to quote, could be summarised as :—

"The greatest blessing a man can enjoy is the power of doing good."

#### THE FOREGROUND AND THE PRESENT ERA

Those personalities whose careers I now portray are happily still with us and I hope may remain so for many years. It is an invidious task to make a selection amongst the many who have retired from active work, so I have restricted my list to three.

To *George Carmichael Low* this Society owes an inestimable debt. He was born in Monifieth, Angus, in 1872. Educated at St Andrew's University, he completed his medical studies at Edinburgh, gaining first-class honours in 1897 and the Gold Medal for his Thesis in 1910.

He was also awarded the Kingsley Medal in 1929. He has always remained a most loyal son of this University where he derived his first inspirations from Greenfield, and subsequently he became one of the first disciples of Manson at his School of which he was appointed director. There he performed his chief original scientific work on the development of *Filaria bancrofti* in the mosquito, studied in celloidin sections, and he succeeded for the first time in tracing the migration of the larval filaria through the head into the proboscis of that insect. In 1900 he took part in Manson's historical experiment at Ostia in the Roman Campagna. Together with Dr Sambon and Signor Terzi he lived in a mosquito-proof hut during the most malarial autumn months. Whilst all the surrounding Italian peasants were stricken with fever, the health of the hut party remained perfect. Low was responsible for the organisation and conduct of the experiment, a task which he performed with native thoroughness, but not without some difficulty. In 1901 he worked for a period on filariasis in the West Indies and British Guiana, and then in 1903 he served with the Royal Society's Commission in Uganda and made a study of *Acanthocheilonema perstans* and assisted in unravelling the trypanosomiasis problem. Dr Low was one of the first secretaries of this Society from 1912 to 1920. During the first world war he conducted its affairs almost single-handed. To him more than any man we owe the creation of Manson House as the Headquarters of this Society in London; he helped to design the Lecture Hall of which we are so proud, and he adorned it by the munificent gift of the carved rostrum which is such a feature of our meeting place. Finally, Dr Low was President of the Society for the record span of four years—1929-1933. He has won fame not only as a teacher of tropical medicine but as an ornithologist of some distinction.

*Robert Thomson Leiper* has achieved world fame as a helminthologist and is founder and editor of the *Journal of Helminthology*. He was born in 1881 at Kilmarnock. Already as a student at Glasgow University he had attracted attention by his helminthological ardour and was engaged with Professor Hamilton in making some valuable discoveries in helminthic diseases of sheep. Whilst still in his early twenties he was selected by Manson as the most suitable candidate for lecturer in Helminthology at his School. For a space of time he worked with Professor Looss of international fame in Cairo. He has made many expeditions to the tropics to conduct research. Thus he went to the Gold Coast in 1905, to Nigeria in 1912, to China in 1914, and British Guiana in 1921. It is unnecessary to point out that he has made many first-class discoveries, such as working out the life history of *Loa loa*, that of the guinea worm with a description of the long-sought male, but undoubtedly his greatest achievement has been the tracing of the full life story of the Bilharzia in Egypt in 1915 and his masterly demonstration of the existence of the two species—*Bilharzia haematobia* and *Bilharzia mansoni*. For this piece of work

he was awarded the Fellowship of the Royal Society. Professor Leiper, who has now retired to his farm in Strathaven, is generally regarded, not only as our premier helminthological expert, but also as a good all-round man of affairs.

Now finally, to complete our list, is one who, like St George, has fought the dragon and won. *Sir Malcolm Watson*, an enthusiastic son of Glasgow, was born at Bridge of Allan in 1873 and was educated at Glasgow University and at University College, London. He is well known all over the world for his anti-mosquito work and for being the inventor of "species sanitation." Sir Malcolm was a friend and disciple of Ronald Ross, so that it is appropriate that in later years he should become director of the Ross Institute, and thus has been enabled to play a prominent part in world-wide anti-malaria campaigns. He has spent thirty years in Malaya, commencing in Klang in 1901. He was the inventor of special anti-larval oils as well as the method of subsoil drainage in ravines. By so doing, and thus altering the environment, he was able to get rid of *Anopheles maculatus*, the chief vector of malaria in the foothills of Malaya. This was the starting-point of "species sanitation." Sir Malcolm has been generally acknowledged the chief authority on malaria prevention, and his services have been solicited by many Governments, and therefore he has travelled widely. His book, *Prevention of Malaria in the Federated Malay States*, is a standard work.

My task is now completed, and I think that what I have been able to record serves to prove the truth of my contention that Scotland as a whole, and your University in particular, have contributed greatly to the advance of tropical medicine. As Scotsmen invariably rise to the top, it may be noted that fully one-third of the number of Presidents of this Society have been of your race. I regret that I have been unable to include all the names I should like to have done, but it is invidious sometimes to praise the living. Did not your national poet exclaim :—

" Oh wad some power the giftie gie us  
To see oursels as ithers see us !  
It wad frae mony a blunder free us."

It would not be an exaggeration to state that you have at present a fair share of talent and you are specially fortunate in having these veterans of the Indian Medical Service—Glen Liston and E. D. W. Greig—still with you.

" The heights to which great men have reached  
Were not attained by sudden flight  
But they, while their companions slept  
Were toiling upward in the night."



# THE CHILD'S INHERITANCE \*

## HEREDITARY, PRE-NATAL AND NATAL INFLUENCES

By J. L. HENDERSON, M.D., F.R.C.P.E.

WHEN the Director of Post-Graduate Studies asked me to give an Open Lecture on a subject of wide biological interest, it occurred to me that we might consider together some of the hereditary and environmental influences which constitute the child's inheritance.

I often think that medical students, who necessarily obtain most of their clinical experience by studying children in child welfare clinics and hospitals, do not visualise the child in his true context. They see a child of a certain age and are taught to assess its state of health, and give scant consideration to the fundamental influences of heredity and environment which have made that child what he is. Many of us who call ourselves *pædiatricians* too often ignore these influences also. The family doctor has a better opportunity than the rest of us of seeing the child in his true perspective, for he knows his collaterals and many of his antecedents, the stock of which he is an expression; and he is familiar with his environment—economic, social, intellectual, tempermental and moral. The family doctor's defective knowledge of scientific detail is well compensated by his wide biological outlook.

### HEREDITY

Those of us who are concerned with the study and practice of child health cannot fail to be impressed by the profound influence of heredity, for not only are the child's soma and psyche cast in the general mould of his antecedents, but a host of individual family traits manifest themselves also. I am not qualified to embark on an exposition of the laws of heredity, and will confine myself to a few general observations in the field of genetics. This science has thrown a flood of light on many biological problems since Father Mendel's laws of heredity were revealed to the World in 1900, thirty-five years after their publication in the journal of a local natural history society in Moravia.

May I remind you that the paternal and the maternal set of chromosomes each contains a complete assortment of genes. Each hereditary trait is thus influenced by a pair of genes, one from each parent, or by several pairs of genes. As a rule, both members of a pair of genes have a similar function, tending to produce the same trait in the organism they help to form, and the resulting individual is considered homozygous for that trait. If, however, as a result of mutation in one of a pair of genes, or in an antecedent gene, whereby

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the trait produced by it becomes abnormal, the two members of the pair of genes have a dissimilar function. In these circumstances the normogenic gene tends to produce a certain character in a normal manner and the mutant partner tends to produce it in an abnormal manner, and the individual is heterozygous for the trait in question; one of the genes is dominant and the other fails to express itself and remains recessive. Recessive genes cannot manifest themselves in a heterozygous individual, only if united with an equivalent recessive gene in a homozygous person. In heterozygous individuals the genetic constitution, the genotype, cannot be recognised because the dominant gene determines the configuration, the phenotype, while the recessive gene remains suppressed. The phenotype is all that matters to the individual, but his genotype and that of his partner determines the genetic constitution of the offspring.

Since planned breeding experiments cannot be undertaken in man it is often very difficult to unravel the various modes of inheritance, or even to be sure that certain traits are inherited at all. Great care must be exercised, therefore, in ascribing human traits to the known modes of inheritance on the basis of isolated and short pedigrees. There is no doubt that in medicine facts of great diagnostic and prognostic value can often be revealed by a painstaking compilation of the pedigree of an individual. Unfortunately, the preparation of an accurate pedigree is usually impracticable, but if obtained, the more obscure modes of inheritance can be interpreted only by experienced geneticists. Crew (1947) has emphasised these difficulties by stating that "to obtain full and accurate information concerning the illnesses and abnormalities of three generations of a family is an impossibility in the great majority of instances." He believes that the country-wide systematic preparation of pedigrees by genetically informed general practitioners, and the establishment of an institute where these could be received, pooled and interpreted, would rapidly advance knowledge of human genetics in relation to clinical medicine.

**THE DOMINANT MODE OF INHERITANCE.**—Persons with a dominant hereditary gene show the corresponding character, whether they are homozygous or heterozygous. If they marry a normal partner, half the offspring can be expected to carry and show the trait, I say "can be expected," and the other half do not inherit it. The children who do not show the character can expect, I say "can expect," normal offspring if their partners are normal. Congenital ptosis, for instance, is usually a dominantly inherited character which appears in every generation, being transmitted directly from the affected parent to one half of the children. There are exceptions to the rules of dominant inheritance as I have hinted, since many pathogenic dominant genes manifest themselves irregularly, indicating that the effects of abnormal genes may be modified. In pedigrees with dominant abnormal traits the phenomenon of a "skipped" generation has often been observed. It may be due to reduced expressivity or to reduced penetrance of the gene.

*Reduced expressivity* may cause only a minimal abnormality necessitating the use of scientific method for its detection: for instance, spherocytosis, which is a disease transmitted according to the law of dominant inheritance, may remain unsuspected until increased fragility of the erythrocytes is demonstrated.

In *reduced penetrance* fewer than the expected number of offspring display the relevant character, even in minimal form. Many genes responsible for the transmission of dominant traits in man have reduced penetrance: in diabetes mellitus, a dominantly inherited disease, the penetrance is apparently only about 10 per cent.

In Recklinghausen's neuro-fibromatosis the penetrance is high, but the expressivity variable, for, though the disease manifests itself in every individual who inherits the gene, some may show all the manifestations of the disease and others only café-au-lait spots. The expressivity and penetrance of an abnormal gene is clearly of great import to the carrier, for it may determine whether he will be crippled or healthy.

Harelip and cleft palate is another example of conditioned dominant inheritance. Fogh-Andersen (1942) of Copenhagen recently published an important monograph on *The Inheritance of Harelip and Cleft Palate*, based on a study of 703 patients drawn from the whole of Denmark. He concluded that harelip, with or without associated cleft palate, has no genetic connection with cleft palate occurring as an isolated malformation. The former is more common in males and the latter in females. The incidence among relatives greatly exceeded the average incidence in the general population in both types of malformation; but, whereas most cases of harelip, with or without cleft palate, appeared to be hereditary, many cases of isolated cleft palate seemed to be non-hereditary. Analysis of the pedigrees showed that the most likely interpretation of the manner of inheritance of the harelip group was "conditioned dominance, with a higher manifestation in males"; while isolated cleft palate seemed to be inherited as a "simple dominant, with failing penetrance and a higher manifestation in females."

Fortunately, it is rare for a pair of abnormal dominant genes to occur in an individual. In such circumstances, the abnormal trait will be likely to manifest itself in a much grosser form than in a heterozygous person, and often proves lethal, causing miscarriage or intrauterine death. For instance, Mohr (1934) quotes the case of a certain type of brachyphalangism, affecting the second fingers and toes, which occurred in six generations of a family as a dominant trait. The slight deformity was of no consequence to the heterozygous individuals affected, but when two heterozygous cousins married, one of their children was apparently homozygous for this abnormal gene and was a cripple with multiple osseous malformations, among them complete absence of fingers and toes.

THE RECESSIVE MODE OF INHERITANCE.—A person heterozygous for an abnormal recessive gene appears normal, and produces normal offspring with a partner who has two normal genes for the trait in question. If, however, such a person marries another heterozygous person like himself, one-fourth of the offspring of this apparently normal couple may be expected to be homozygous and to manifest the abnormal trait. The other three-fourths appear normal, but the genotype is normal in only one-fourth, and one-half are heterozygous like the parents. If the abnormal gene is rare in the general population, the chance of heterozygous carriers marrying one another is remote, unless a heterozygous carrier of the abnormal gene marries a relative ; in such circumstances there is a very much greater chance of encountering an individual of the same genotype. Pædiatricians know well that consanguineous marriages greatly favour the manifestation of recessive traits, for they cannot fail to notice the relatively high incidence of consanguinity of the parents of children with rare hereditary diseases. Among the many rare diseases produced in this way, which I have seen, the excessively rare type of hæmorrhagic diathesis caused by a complete absence of fibrinogen in the blood springs to mind : there was no family history of bleeders in the " L " family until second cousins married, and two of their five children, a boy and a girl, exhibited this very rare type of congenital bleeding disease. No doubt the parents each carry a mutant recessive gene concerned with fibrinogen production, which they have inherited from a common ancestor, and which probably would never have expressed itself if no consanguineous union had taken place. Since gene mutation occurs in both directions, from normal to abnormal and ultimately, after a variable number of generations, from abnormal back to normal, rare mutant genes in many stocks never express themselves at all.

It is comforting to know that the chances of the offspring of a person affected with one of the rare recessively inherited diseases manifesting the condition are remote, for, although all will carry the abnormal gene, all will be heterozygous. This is particularly true if the partner was born in a distant community, since the chance of unknown consanguinity is thereby greatly diminished. The higher incidence of recessively inherited diseases in closed communities where consanguinity is inevitably more common is well known.

OTHER MODES OF INHERITANCE.—I do not propose to discuss the various sex-linkage modes of inheritance or other more obscure modes of transmission. Hæmophilia is, of course, a totally sex-linked recessive mode of inheritance : in pooled pedigrees of hæmophilia there is a significant deficiency of females, probably because the homozygous females usually die *in utero*.

I would emphasise the fact that some abnormal traits which appear to be clinical entities need not necessarily be transmitted by the same mode of inheritance. Microphthalmia, for instance, may

be a dominant, a recessive, or a sex-linked recessive trait. It may be dangerous, therefore, to draw definite conclusions from the study of a small number of human pedigrees.

**DYNAMIC GENETICS.**—I will say little about dynamic genetics, the relatively new field of genetics concerned with the action of the normal or abnormal gene on the developmental processes which lead to the finished trait. It attempts to explain how and when abnormal genes deflect the course of development into channels which lead to abnormal results. Studies explaining the embryonic origin of hereditary anomalies have often made it possible to understand apparent inconsistencies in the laws of heredity, by demonstrating that the mode of action of a certain abnormal gene is not to be sought in the trait recognisable at birth, but in a pathological process of early embryonic development. Experimental embryology has demonstrated that certain areas of the embryo exercise a greater regulatory influence on morphogenesis than others. Such areas of dominating influence are called organisers, and they exercise their influence by producing certain chemical substances which bring about the differentiation of tissues. Some genetic effects can best be explained by assuming that an organiser is injured by the abnormal gene, since injured organisers set up a chain of abnormal reactions in subsequent stages of embryonic development. Experimental injury of an organiser may have the same effect as an abnormal gene. Hereditary congenital abnormalities may also be produced by the pre-natal degeneration of tissues which originally were normally formed: intrauterine amputations are now considered to be due to vascular anomalies, like the associated amniotic bands which were formerly thought to produce them. Experimental embryology still has much to contribute to a better understanding of genic action.

#### PRE-NATAL ENVIRONMENTAL INFLUENCES

It must not be assumed, as there was a tendency to do some years ago, that all congenital anomalies are genetically determined, or that subnormal development and intrauterine death usually have a similar origin. Environmental interference with pre-natal development may cause all these disturbances. Nutritional deficiencies, pre-natal infection, endocrine, actinic, chemical, mechanical factors, may all have a baneful influence on the growing organism.

**NUTRITIONAL DEFICIENCIES.**—Adequate nutrition of the embryo is indispensable for optimal development. Nutrition may be interfered with by various factors, such as faulty implantation of the ovum, diseases of the placenta, dietary deficiencies, or the transmission of toxic substances to the embryo. Most of these causes are maternal in origin, but the cause may lie in the embryo. Starvation in early pregnancy may cause death of the embryo; later in pregnancy death is less likely, but the incidence of stillbirth will be increased and the birth-weight of the young diminished. General starvation leads to

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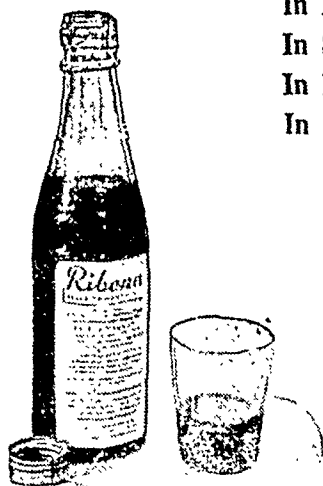
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sterility: Clement Smith (1947) has pointed out that one-half of the women living in The Hague and Rotterdam in the starvation winter of 1944-45 had amenorrhœa, and 50 per cent. of the other half had irregular menstruation.

Mall (1908), the eminent embryologist, believed that ova are likely to be converted into monsters if their normal connection with the maternal organism is interrupted. The fact that in ectopic pregnancy normal ova frequently develop abnormally supports the theory of faulty implantation, with subnormal nutrition, as a cause of malformation.

It is impossible at present to estimate how frequently maternal dietary deficiency is a factor in the ætiology of congenital anomalies, but experiments and observations in this field have shown that a lack of certain dietary elements which cannot be synthesised by mother or embryo may simulate abnormal genic action, not only by producing comparable finished traits, but also by inducing similar pathological manifestations in the embryo. Congenital malformation can be induced by omitting single nutritional elements, such as minerals and vitamins, from the maternal diet, while maintaining an adequate caloric intake; but to disturb formation of the embryonic organs, the deficiency must affect mother and offspring in the organogenetic period—the first two months of gestation. Moreover, a borderline deficiency is required to induce malformations, for a slight increase in the deficient dietary factors may produce normal offspring, while a further reduction may cause embryonic death. Maternal vitamin A deficiency, for example, interferes with normal reproduction. It may cause sterility, congenital anomalies, foetal death or the birth of dead or weakly young. Warkany (1947) and his collaborators, in the course of a series of brilliant experiments on the ætiology of congenital malformations, have demonstrated that a high incidence of congenital malformations can be induced in rats by feeding the mothers on a diet lacking riboflavin, but normal in all other respects. They showed that the malformations could be prevented by the addition of riboflavin as late as the thirteenth day of gestation. Histological sections in other specimens showed that the malformations were present in cartilaginous structures on the fourteenth or fifteenth day. It was assumed, therefore, that in the thirteen or fourteen day-old rat embryo there is a critical stage when the presence or absence of sufficient riboflavin has a decisive influence on embryonic development. At this time most of the affected parts of the skeleton undergo rapid changes from undifferentiated mesenchymal structures into well differentiated skeletal elements. Since the young produced on a riboflavin deficient diet had grown satisfactorily, it would appear that a higher riboflavin level is needed for tissue differentiation than for growth. A deficiency of riboflavin is thought to interrupt normal developmental processes because it is a constituent of a number of enzymes essential for tissue respiration.



Increasing attention has been paid in recent years to the ill effects on the developing child of suboptimal nutrition in pregnancy. Several large-scale controlled studies have been undertaken in which the result of pregnancy in a group of women who received an optimal diet was compared with the result of pregnancy in a group of women of inferior economic status who received a deficient unsupplemented diet. The investigations of Ebbs and his colleagues (1941, 1942) in Toronto, Burke and her associates (1943, 1945) in Boston, and the People's League of Health (1942), and Balfour (1944) in England, all showed a reduction in the frequency of miscarriage, premature birth, stillbirth and neonatal death in the group on an optimal diet.

In a study of diet during pregnancy Baird (1947) of Aberdeen found that women in the Registrar-General's Social Class I (professional and well-to-do) consumed much more meat and fruit, many more eggs, and more milk than women in Social Classes III to V, the low income groups. Moreover, those in the high income group took vitamin supplements much more conscientiously. McCance *et al.* (1938) also found that in poor districts, where the amount of money spent on food was low, the diet of expectant mothers was deficient in protein, especially animal protein, calcium, phosphorous, iron and thiamin. When the income rose, there was increased consumption of milk, fruit, meat and vegetables, and decreased consumption of bread.

In a recent paper on the relation of foetal mortality to social class Baird (1947) found not only the diet, but the health and physique of the higher income groups to be much better than that of the lower income groups. The reproductive performance in the high income group was superior to that in the low income groups. The stillbirth rate, after making allowance for the different age of child-bearing, parity, etc., in the various groups, was two to three times greater in the low income groups than in the high income group. Unexplained intrauterine deaths and prematurity were much higher in the low income groups, and neonatal death considerably higher. During the years 1939-44 there was a sharp fall in the stillbirth rate in Scotland, particularly in the category of unexplained intrauterine death, and also in prematurity. Baird believes, with justification, that the fall in the stillbirth and prematurity rates during these war years was chiefly due to improved diet in pregnancy. The government's policy of supplementing the diet of expectant mothers with milk, an excellent source of first-class protein and of calcium, and of ensuring a fair distribution of food by rationing, would seem to have been abundantly justified. No doubt the improved economic status of the low income groups during the war years also contributed to the improvement.

Two interesting studies have recently been published concerning the effect on the offspring of severe war-time starvation of expectant mothers. The effects of starvation in Leningrad during the 1942 siege were analysed by Antonov (1947), and those in Rotterdam and The Hague during the Dutch hunger-winter of 1944-45 by Clement

Smith (1947). Antonov found that the stillbirth-rate in the Newborn Department of the Leningrad State Pædiatric Institute had risen to twice the pre-war figure; it was 5·6 per cent. of all births in 1942. The premature birth-rate, based on a birth-length of less than 47 cm. (normal birth-length 51 cm.), reached the high figure of 41·2 per cent. The average weight of full-time infants was 500-600 gm. ( $1\frac{1}{4}$  lb.) less than pre-war; this fact contributed to a considerable extent to the high figure of 49·1 per cent. of infants who weighed less than  $5\frac{1}{2}$  lb. at birth, and necessitated the adoption by Antonov of the more reliable birth-length standard of prematurity. The vitality of the newborn was diminished and the skull bones were often abnormally soft, while morbidity and mortality in the newborn period were unusually high. In the terrifying conditions of a prolonged siege under modern conditions of warfare emotional factors would no doubt contribute to these abnormal results of pregnancy; nevertheless, severe malnutrition must have accounted for the vast majority of these abnormalities, since Antonov showed that expectant mothers with free access to food, such as cooks and canteen workers, had normal obstetrical results comparable with pre-war years. Although lacking dietary details, and the great virtue of being controlled, Antonov's study is of interest to nutritionists and pædiatricians.

Clement Smith found in Rotterdam and The Hague that there was a considerable diminution of the birth-weight and a slight diminution of the birth-length of the newborn, when compared with the pre-war figures. It is perhaps surprising in view of the very harmful effect of severe malnutrition demonstrated by Antonov, and the results of other nutritional studies in pregnancy, that there was only a slight increase of prematurity, and no increase in the incidence of stillbirth, neonatal death, or congenital defects. Since the daily caloric intake of expectant mothers fell to 1145 and the protein to 34 g. in January 1945, one would have expected the ill-effects of such severe starvation to be more clear-cut. It would be a mistake, however, to allow the results of this uncontrolled investigation to throw doubt on the importance of optimal nutrition in pregnancy. The fact that most of the women were sterile during the starvation period suggests that the expectant mothers must have been the women with a physique above average, the women with the best obstetrical prognosis. Moreover, the diet was not a starvation one during the whole period of pregnancy, and it soon became adequate after the liberation. Smith's study, therefore, though it yielded much valuable information about the effects of malnutrition, cannot be compared with the others I have quoted; but in Smith's own words it did emphasise "the necessity for great caution in the evaluation of maternal-fœtal aspects of nutrition. Also, that data regarding the duration of maternal nutritional depletion, and the specific dietary elements involved, would appear to be of essential importance in any study of the problem."

**PRE-NATAL INFECTIONS.**—Such infections have often been discussed as possible sources of congenital malformations, but no proof has been forthcoming until recently. In 1941, Gregg (1942), an Australian ophthalmologist, discovered that maternal rubella in the first two months of pregnancy causes various congenital defects in the offspring, notably congenital cataract, congenital malformations of the heart, deaf-mutism and mental defect. Gregg's observations and deductions were soon confirmed in various parts of the world. It is now recognised that the severity of the disease is of minor importance in the ætiology of the malformations; in one case showing typical congenital malformations the mother was unaware of having been ill during the pregnancy, but two of her children had rubella during the second month of her pregnancy so that sub-clinical rubella may be assumed. Children whose mothers have rubella after the second month of pregnancy do not have malformations, because in man the organogenetic period is terminated by the end of the second month, but almost 100 per cent. of mothers who contract rubella in the first two months of pregnancy give birth to infants with congenital anomalies. It is assumed that the virus invades the cells which are about to divide and differentiate rapidly, thus inhibiting their normal development. Possibly the virus may chiefly affect the embryonic vascular system. Attempts have been made to discover whether other virus infections can injure the embryo in a similar way; no such causal relationship has been found, but the future may provide many surprises in this field.

Pre-natal infection with the protozoon toxoplasma may cause congenital malformations, but there are no major developmental defects because the disease affects the fœtus at a later stage of pregnancy than the organogenetic period.

**MECHANICAL FACTORS.**—Less emphasis has been placed on mechanical factors as a cause of congenital malformations since the discovery of other possible injurious agents. True malformations, such as spina bifida, cannot be due to spatial impairment since they arise in the organogenetic period, but abnormal intrauterine position of the fœtus at later stages of pregnancy may cause abnormal mechanical forces to operate on certain parts of the fœtus, with the production of congenital malformations. Asymmetries of the head, deviation of the jaw to one side resulting from compression by an elevated shoulder, and genu recurvatum are examples of such malformations. Such acquired congenital malformations, unlike organogenetic malformations, usually show spontaneous improvement after birth, since the abnormal mechanical force which produced them is no longer operative.

**ENDOCRINE FACTORS.**—Endocrine imbalance produced experimentally in animals, such as by the administration of large amounts of sex hormones, will produce congenital malformations in the offspring. Several investigators have recently pointed out that there

is an abnormally high incidence of congenital malformations in the offspring of diabetic and pre-diabetic mothers. It is thought to be the associated endocrine imbalance, and not the diabetes *per se*, that causes the subfertility, congenital malformations, and high intrauterine death rate in diabetes.

ACTINIC FACTORS.—It is well known that röntgen and radium rays may interrupt embryonic or foetal differentiation and growth. Zappert (1926) collected 20 cases of foetal microcephaly which he regarded as röntgenogenic; in all except two cases the mother was exposed to irradiation in the first trimester of pregnancy. Following this and other warnings of the danger of irradiation in pregnancy, radiotherapy in pregnancy became a rare procedure.

CHEMICAL FACTORS.—Little is known about the rôle of chemical factors in the ætiology of mammalian malformations, but it is likely that such factors may interfere with normal organogenesis, since such interference can be induced by chemical factors in lower animals. For instance, the high rate of congenital malformations in chicks in South Dakota, in the Middle West of the United States, was found to be due to a toxic substance called selenium. Franke *et al.* (1936) isolated selenium from the grain, grown locally, on which the mothers of the chicks were fed.

#### SOME EFFECTS OF ABNORMAL BIRTH

The stage of transition from the relatively uniform intrauterine environment of dependence, to the more variable extrauterine environment of independence, is one of special danger. Premature birth and respiratory failure are the commonest causes of death and crippling, while intracranial trauma, though less common than formerly, is still a common incident. The frequency of all these abnormalities can be reduced by raising the economic and social status of the lower income groups in the community, thus improving the physique of girls and women, and the diet of expectant mothers. I have already pointed out that these are the essential prerequisites for drastically reducing the prematurity rate, and since prematurity predisposes to respiratory failure, the incidence of that grave accident would also be diminished.

It is well known that intracranial birth trauma may permanently damage the central nervous system, but less often realised that the prolonged anoxia associated with respiratory failure is possibly a more common cause of such crippling. There is some difference of opinion about the ultimate prognosis in the prematurely born, a fact which emphasises the necessity for large-scale controlled follow-up investigations of premature infants to be undertaken. I believe the physical and mental prognosis shows little impairment in premature infants with a birth-weight of over 4 lb., but pronounced impairment in very premature infants with a birth-weight below 3 lb.

The most reliable follow-up study of very premature infants is probably that of Hess (1947) and his associates, an outline of which was communicated to the International Pædiatric Congress in New York last July. In the twenty-five years' period since the opening

TABLE I

*Developmental Ratings in 201 Cases of Prematurity with a Birth Weight below 2lb. 12½ oz. (Hess et al., 1947).*

Rating.	Development.	
	Physical.	Mental.
Satisfactory . . . . .	160 (80 per cent.)	170 (85 per cent.)
Poor . . . . .	18 (9 per cent.)	20 (10 per cent.)
Bad . . . . .	22 (11 per cent.)	10 (5 per cent.)

of the famous prematurity unit at the Sarah Morris Hospital in Chicago in 1922 a total of 259 infants with a birth-weight between 1 lb. 10 oz. and 2 lb. 12½ oz. were discharged, the remaining 75 per

TABLE II

*The Incidence of Residual Central Nervous System Pathology in 201 Cases of Prematurity with a Birth Weight below 2lb. 12½ oz. (Hess et al., 1947).*

Degree.	Incidence.
Slight . . . . .	1 (½ per cent.)
Moderate . . . . .	9 (4½ per cent.)
Severe . . . . .	19 (9½ per cent.)
Total . . . . .	29 (14½ per cent.)

Type of Severe Residual Damage.	Incidence.
Mental defect with or without spasticity	12 (6 per cent.)
Spasticity without mental defect . .	3 (1½ per cent.)
Bilateral blindness . . . . .	3 (1½ per cent.)
Familial amaurotic idiocy . . . . .	1 (½ per cent.)

cent. of the infants in this weight-group having failed to survive. May I remind you that the upper weight limit in this group corresponds with a gestation period of twenty-eight weeks, the age at which, according to the traditional obstetrical phrase, "the foetus is presumed to become viable." The question is often asked: "Are very small

premature infants worth saving?" so let us review briefly the results of this unique and most important follow-up by Hess and his colleagues. Thirty-two of the 259, shall I say "pre-viable," infants who were discharged from the Sarah Morris had died, and 201 were contacted and examined at ages varying from six months to twenty-two years. The follow-up showed a fairly high incidence of physical and mental defect (Table I). Abnormalities were concentrated in the eyes, the nervous system, the skeleton and the circulatory system. Twenty-eight and a half per cent. had showed evidence of intracranial pathology in the neonatal period. Half of these showed no evidence of central nervous system pathology and half did; of the 29 who did, 19 showed

TABLE III

*The Incidence of Eye Pathology in 201 Cases of Prematurity with a Birth Weight below 2 lb. 12½ oz. (Hess et al., 1947)*

Extraocular Defects.	Incidence.
Convergent Strabismus . . . .	30 (15 per cent.)
Divergent Strabismus . . . .	9 (4½ per cent.)
Total . . . . .	39 (19½ per cent.)

Intraocular Defects.	Incidence.
Retrolental fibroplasia . . . .	5 (2½ per cent.)
Cataract . . . . .	5 (2½ per cent.)
Optic atrophy . . . . .	2 (1 per cent.)
Total . . . . .	12* (6 per cent.)

\* Seven showed signs of intracranial pathology in the neo-natal period.

severe, 9 moderate and 1 slight involvement in the form shown in Table II. Nineteen and a half per cent. had strabismus, mostly convergent; 6 per cent. showed intraocular defects, seven-twelfths of these being in children who showed signs of intracranial pathology in the neonatal period. The nature of the ocular defects is shown in Table III. Five and a half per cent. of the cases had suspected congenital heart disease.

I leave it to you to judge whether it is worth trying to save "pre-viable" infants. I certainly think it is when 80 per cent. show satisfactory physical development and 85 per cent. satisfactory mental development.

Clearly, the inheritance of many children, too many, is profoundly influenced by obstetrical complications and their pre-disposing factors.

## INHERITED IMMUNITY

In the early months of life the infant is protected from the ravages of most bacteria by antibodies inherited from the mother, and this passive immunity is gradually replaced by the development of spontaneous active immunisation. In anthropoids and rodents the placenta is hæmochorial and the placental barrier is very thin, consisting of only one layer of cells. It is thus permeable to antibodies, which are contained in the relatively small globulin molecules. Thus, the child obtains his maternal antibodies principally through the placenta before birth, though a relatively small proportion of antibody is acquired through the colostrum after birth. Brambell, Hemmings and Rowlands (1947), in a preliminary communication just published, present experimental evidence in rabbits which suggests that antibodies can pass to the embryo by a route other than the hæmochorial placenta, and they suggest that current views regarding the mode of transmission of antibodies to the foetal infant may have to be modified. In other mammals, such as the ungulates, the placental membrane is thicker and it is impermeable to antibodies. In these species all the antibodies are obtained through the colostrum after birth so effectively that their titre in the serum of the young may equal or exceed that of the mother a few hours after the first feed.

Among the commoner antibodies which pass the placenta are those for diphtheria and the various virus diseases such as measles. This passive immunity lasts about six months and accounts for the infrequency of these diseases before that age. A more fleeting resistance is demonstrable against the pneumococcus, influenza bacillus, streptococcus and staphylococcus. The titre of specific coliform antibodies is much lower in the serum of the infant than in that of the mother, and unless the mother has a fairly high level the infant has none; this may explain the undue susceptibility of the newborn infant to severe coliform infections, such as meningitis, which seldom occur after the first month or two of life.

## CONCLUSION

I have spoken at length about the child's inheritance, genetic and environmental, up to the time of birth, and I have concentrated on the baneful influences rather than the physiological. Fortunately, the vast majority of infants are born without pathological inherited traits, and without having suffered any ill effects from potentially harmful environmental influences. The general pattern of the child's post-natal development, physical and mental, is pre-ordained by his genotype, but his innate characteristics are now influenced, to a greater degree than before birth, by environmental factors of ever-increasing range and complexity.

In the course of a single lecture one can discuss only a few aspects of the child's inheritance, and I have concentrated to-day on recent advances in knowledge in the fascinating field of pre-natal life.

## ACKNOWLEDGMENTS

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I also wish to thank Dr Julius Hess of Chicago and his associates for permission to refer to their recent follow-up study of very premature infants.

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# A HUNDRED YEARS OF CHLOROFORM\*

By DOUGLAS GUTHRIE

I HAVE been asked to address you at this centenary meeting on "The Discovery of Chloroform Anæsthesia," and no doubt the University has acted wisely in apportioning the duty to one who is neither an anæsthetist nor an obstetrician, but simply a worker in the neutral field of history.

It is good to praise famous men and to recall great achievements, and surely the discovery of chloroform anæsthesia by Professor James Young Simpson was one of the most important advances, as well as one of the most dramatic episodes, in the long history of medicine, which we do well to celebrate upon this, its hundredth anniversary. As we do so, we may find it hard to realise that the discovery was so long delayed, and that only so recently as the middle of last century was surgery completely revolutionised by the introduction of anæsthesia and antiseptis.

The quest for some means of relieving pain had been pursued down the ages since prehistoric times. *Nepenthe*, used by Helen of Troy, was followed by *mandragora*, a drug which retained its popularity for many centuries. Other pain-relieving agents—opium, and henbane, and various "drowsy syrups," as well as physical means, such as freezing or pressure, were employed with very varying degrees of success.

Animal magnetism, or mesmerism, was the anæsthetic method which held the popular imagination and also the attention of surgeons in this country about the middle of last century, when there arrived from America news of the spectacular use of ether by inhalation. The first public demonstration of the value of ether anæsthesia in surgery was given by William T. G. Morton at Boston, on 16th October 1846. There were other claimants to the priority of the discovery—Crawford Long, Horace Wells, and Charles Jackson. There is no need to revive this complex controversy, so widely publicised a year ago. Suffice it to say that our present festival in no way detracts from the merit due to the American pioneers of ether anæsthesia.

Robert Liston, at University College Hospital, London, is usually regarded as the first to employ ether anæsthesia in major surgery in Britain in December 1846; while James Young Simpson was the first to introduce it into obstetric practice, in January 1847. On hearing of the American discovery, Professor Simpson had written to his brother, "It is a glorious thought; I can think of naught else." Here was the solution to a problem which had intrigued him since

\* Address delivered in the Upper Library Hall, University of Edinburgh, on 4th November 1947, at a reception to celebrate the centenary of the discovery of chloroform anæsthesia by Sir James Young Simpson.

his student days, and now he readily grasped the opportunity of testing its efficiency. As he continued to use ether, it became apparent to Simpson, and to many others, that this was not yet the ideal anæsthetic. It was uncertain in action, irritating to the air passages, and required special apparatus for its administration. Simpson resolved that he would find some anæsthetic which would be free from such disadvantages.

He inhaled all manner of gases and vapours, and it is said that on one occasion at least, before his discovery, he rendered himself unconscious, greatly to the alarm of his family. In his search for a new anæsthetic he enlisted the services of his assistants, Keith and Matthews Duncan. On many an evening, when each day's work was over, the trio sat around his dining-room table at 52 Queen Street, engaged in a strange but heroic experiment upon themselves. Early each morning, Simpson's next door neighbour, Professor Miller, would call to ascertain the results, or, as he himself remarked, "to find out whether everyone was still alive."

The little team of investigators had been at work for several months, and a variety of substances had already been tested. Shortly before the night in question, David Waldie of Liverpool had mentioned to Professor Simpson that it might be worth while to try the effect of perchloride of formyle, or chloroform. Waldie, a medical man who had become a chemist, deserves credit for his suggestion, although he made no experiments on his own account.

A small quantity of chloroform had been prepared for Simpson by the professor of chemistry, William Gregory, but it had been laid aside as it appeared heavy and unpromising. On the night of the discovery, after several substances had been tested without result, this little phial was searched for, and found under a heap of waste paper. Simpson himself was the first to inhale it, and his companions followed his example on observing that it seemed effective. Naturally he was also the first to regain his senses, and the thought prominent in his returning consciousness was that something "far stronger and better than ether" had been discovered. Then he noticed that Matthews Duncan was snoring in his chair with open mouth and staring eyes, while Keith, having reached only the stage of excitement, had slipped under the table and was kicking it vigorously. Each of them on recovery echoed Simpson's satisfaction with the effect of the new agent.

The witnesses of this strange scene, who must surely have been much alarmed, included Mrs Simpson, her sister Miss Grindlay, and her niece Miss Petrie. When further trials were made, Miss Petrie insisted upon inhaling the drug, and thus became the first woman subjected to its influence.

Some few days later in the Royal Infirmary of Edinburgh, Professor Simpson administered chloroform to three patients, two of whom underwent operation by Professor James Miller, the third by Mr John

Duncan. The first of them was a highland boy, whose name is unrecorded and who could speak only Gaelic. A large fragment of diseased bone was removed from his arm. He continued to sleep soundly after the operation and felt no pain.

Simpson lost no time in making known his discovery. Within a week, on 10th November 1847, he presented to the Medico-Chirurgical Society of Edinburgh his "Account of a New Anæsthetic Agent." Chloroform rapidly became the anæsthetic of choice, and soon superseded ether in this country and on the continent.

Nevertheless Simpson continued his researches, hoping to improve the method. Every member of his household was now eager to share in the work. At one time Professor Simpson resolved to try the effect of drinking a mixture of chloroform and champagne. Hearing of this, his butler, named Clarke, administered a dose of the potent cocktail to the cook, who promptly fell insensible on the kitchen floor. Clarke rushed upstairs to his master, calling "Come down, sir, come down for God's sake, I've poisoned the cook." Fortunately the victim rapidly recovered.

It seems advisable that one should include in this brief survey some account of the life-story of the discoverer, of whose accomplishment this University may well be proud. Born at Bathgate in 1811, the youngest of a family of eight children, James Simpson climbed the ladder of fame from a lowly rung. From his earliest years he had an insatiable appetite for learning, and even at the village school he was known as the "wise wean." Poor though they were, his father and mother resolved that Jamie would proceed to the University, and this he did at the age of fourteen.

"Thus, I entered Edinburgh University," he told the audience on receiving the Freedom of the City many years later, "very young, very solitary, very poor, and almost friendless." His estimate of the relative values of nourishment and knowledge is shown by an entry in his diary of expenses as a student: Finnan haddies, 2d.; Book on Osteology, 21s. During his student days he was so repelled and shocked by the dreadful scenes of suffering in the operating theatre that on one occasion he actually resolved to abandon medicine and to devote himself to the study of law. Leaving the Infirmary he proceeded to Parliament House with this object in view. Fortunately, his better judgment prevailed. He accepted the existing conditions as a challenge rather than as a deterrent, and it seems probable that from that very day he gave much thought to the clamant need for the prevention and relief of pain in surgery.

After graduating M.D. in 1832, he became assistant to John Thomson, the professor of pathology, and it was Thomson who advised him to specialise in midwifery. In 1840 the Town Council of Edinburgh, by a majority of one vote, appointed him professor of midwifery in succession to Professor Hamilton. He brought great repute to the chair and he contributed very materially to the progress

of midwifery and gynæcology. Nevertheless he did not allow his specialty to monopolise all his energies. A versatility such as his could not accept the limitations of specialist practice.

His advocacy of the control of hæmorrhage by needles in place of ligatures, acupressure, as he called it, brought him into conflict with some of his surgical colleagues. Simpson regarded this discovery as equal to the discovery of chloroform anæsthesia, although acupressure has now become a mere historical curiosity. Another campaign of Simpson's was directed against the evil of large hospitals, the so-called hospitalism. In place of the great solid structures, so conducive to septic infection, he advised the building of small temporary hospitals. His conclusions were not always correct: indeed, he was one of the strongest opponents of Lister's methods. Nevertheless his arguments were always supported by evidence carefully collected.

Nor did he confine his researches to medicine. On archæology he was an acknowledged authority, and he published papers on leprosy in Scotland, on the buildings on Inchcolm, on medical officers in the Roman army, to mention only a few. Well, indeed, might Dr John Brown remark to a friend, as Simpson passed along the street, "There is not one man, but many men, under that coat."

His residence at 52 Queen Street, now known as Simpson House, was constantly filled by numerous patients, distinguished visitors, and post-graduate students, to all of whom he extended a cordial welcome. At every meal, even at breakfast, there were guests, invited and even uninvited.

His well-stored mind and multiple interests made him an ideal host, and he delighted in argument and debate, being gifted with an unusual fluency both of pen and tongue.

In the conduct of his practice he was obliged to undertake many a long and weary journey, but fortunately he had the aptitude for sleeping anywhere and at any time. The short journeys and the daily round he accomplished by carriage, for which Messrs Croall supplied a pair of spirited horses and a coachman who was not always sober. Summoned one evening to Hopetoun House, Professor Simpson wondered why he was taking so long to reach Queensferry, until he discovered that for over an hour he had been driven round and round the garden railing side of Ainslie Place, from which the driver alleged that he could find no way out!

Simpson's address as Promoter at the Graduation Ceremony of 1868 was a masterly performance, and in it he prophesied the discovery of X-rays, remarking that "one day, by means of electric lights, we may render the human body transparent to the eye of the surgeon." Two years before that date he had been the first medical man in Scotland to receive a baronetcy, and it is significant that he chose as his motto: *Victo dolore*. His race was now nearly run. Although he died at the age of fifty-nine, he had crowded into that lifetime a full and varied career.

Of course Simpson did not discover the substance chloroform. That discovery had been made in 1831-32, independently and almost simultaneously by three chemists, Souberian, Liebig, and Guthrie, in France, Germany and America. Chloroform had been used internally in medicine and indeed it is still so used. It is also used very largely to flavour confectionery, and as a solvent in many industrial processes. Simpson, however, was the first to describe and demonstrate its employment as a general anæsthetic.

Others played minor parts in the discovery. David Waldie, for example, the Linlithgow doctor who became a chemist in Liverpool, suggested to Simpson that chloroform was worthy of a trial, but he published no observations of his own, if indeed he made any experiments. Simpson's assistants, Keith and Matthews Duncan, deserve a share of the credit, and it has been alleged that the latter made a personal trial of chloroform before the classic day, just as it is also said that Simpson tested the drug in advance. Such tales may or may not be true, and are of little significance.

One other name, however, deserves mention alongside that of Simpson. Dr John Snow of London, the first professional anæsthetist, introduced many technical improvements, and it was he who administered chloroform to Queen Victoria at the birth of Prince Leopold in 1853.

It is a strange commentary on the times in which he lived that Simpson was obliged to defend anæsthesia against those who objected to its use in obstetrics on religious grounds. He answered the critics in their own tongue, showing an amazing acquaintance with the Hebrew text. The controversy continued for several years, and it was the Royal patronage of the new drug which finally silenced the narrow-minded opposition.

By the medical profession, the advantages of chloroform over ether were at once recognised. For a time, chloroform entirely displaced ether and became almost the only general anæsthetic in use all over the world. It was even stated by some authorities, including Lister, that chloroform was perfectly safe, provided due attention was paid to the respiration. Professor Syme could point to 5000 cases of chloroform administration without a death. Nevertheless reports of deaths in this and other countries shook the original optimism, leading to a revival in the use of ether, to the use of nitrous oxide, and various mixtures of ether and chloroform, and to the introduction of dosimetric methods, as opposed to the uncertain drop method, the so-called "rag and bottle" anæsthesia, so highly favoured in Edinburgh. Perhaps the most beneficial effect of the argument regarding the virtues of this or that anæsthetic or method was the development of anæsthesia as a specialty, and of the anæsthetist, who devoted all his time to this work.

Since its introduction by Simpson a century ago, chloroform has retained its place as a general anæsthetic, although it is no longer

employed in random fashion. Regarding its present use, I am not qualified to speak, and in any case the question was admirably discussed by three eminent anæsthetists this morning. This, however, one may say with confidence, that the very name "chloroform" reflects credit upon the University of Edinburgh. It is right and proper that we should celebrate the birthday of our centenarian. During those hundred years many a sufferer has had reason to be thankful for "the thick, sweet mystery of chloroform," which has transformed an unspeakable anguish into what Henley called, "an immense, complacent dreamery." Looking back, we now salute the memory of James Young Simpson, who, by his discovery of chloroform anæsthesia, achieved immortal fame. *Victo dolore.*

## CHOLESTEROL PLEURAL EFFUSION \*

By THOMAS M. CURRAN, M.D., M.R.C.P. Ed.

ALTHOUGH chronic pleural effusions are of common occurrence, the presence of cholesterol crystals within them is but rarely encountered if one is to judge from reports in the literature. Churton first described this condition in 1882, yet only 32 cases have been subsequently reported, and of these, only 5 appear to have been described in Great Britain. The last recorded cases are those described by Erwin (1941) from Frodsham, and by Evander (1946) from New York.

The nomenclature of the condition has been variously described as cholesterol pleural effusion, cholesterous pleural effusion, cholesterol pleurisy and cholesterol thorax. Of these, I think that the first mentioned is the most accurate description.

It is essentially a chronic condition, showing a marked tendency to recurrence, and its recognition depends on the demonstration of cholesterol crystals which can be easily seen on microscopic examination of the fluid. The latter may be clear or turbid and may be yellow, brown or brownish-red in colour, but it usually possesses a sheen imparted by the cholesterol crystals it contains.

There is no unanimous agreement on the aetiology of the condition which has been found usually in middle-aged adults, predominantly males. Less than half of the cases described showed evidence of pulmonary tuberculosis. The majority of reports mention only a primary effusion, tubercle bacilli being usually absent on direct examination and culture, and only occasionally identifiable following guinea-pig inoculation. One patient died of tuberculous meningitis, although tubercle bacilli could not be isolated from the pleural fluid. Diabetes, syphilis, or a combination of either of these with lung tuberculosis, have occasionally been considered as causal factors.

The clinical picture is that of a benign pleural effusion, with no signs of fever or toxæmia, and although the effusion is usually large, it is often encysted, with marked pleural thickening, and gross pressure symptoms are uncommon. The complaints usually encountered are: slight dragging pain in the affected side of the chest, a dry cough, or slight dyspnoea on exertion.

CASE REPORT.—The patient, a male aged 43 years, was admitted to a sanatorium in England in August 1930 with tuberculosis of his right lung. He was treated conservatively and was discharged in good condition in December 1931. His health remained good until August 1933 when he had two severe hæmoptyses, following which he was admitted to East Fortune Sanatorium on 2nd September of

\* Read at a meeting of the Tuberculosis Society of Scotland, held at Bangour Hospital on Friday, 31st October 1947.

that year. He was then afebrile and in moderate condition, but his cough was troublesome and he brought up mucopurulent sputum which contained numerous tubercle bacilli. The X-ray film showed fairly well-defined infiltrative disease of the upper two-thirds of the right lung with more dense nodular and fibrotic shadowing just above the upper interlobar septum, in the midst of which there was honey-combed cavitation. A right artificial pneumothorax was induced on 4th November 1933, and although the upper lobe was adherent on its mediastinal aspect and was held out by several lateral adhesions, there was a considerable improvement in his general condition, and his sputum became fractional and negative for tubercle bacilli. He was discharged on 5th May 1934 to attend as an out-patient for pneumothorax refills.

His condition remained satisfactory until March 1940, when he became fevered and complained of pain in the right side of his chest. Cough was more troublesome; sputum increased in amount and was tinged with blood.

He was re-admitted to the sanatorium a few days later, when his sputum was found to contain tubercle bacilli again, and his X-ray film showed a rather general lateral collapse of the lung which was adherent at its apex and base, with a complex system of adhesions passing laterally from the lower half of the right upper lobe. There was extensive calcification of the lung disease, but irregular translucencies suggested the persistence of small cavity formation. Fluid covered the right diaphragm, and on aspiration it was found to be slightly turbid, examination of smears showing numerous cells, largely lymphocytes. Tubercle bacilli were not found.

His temperature quickly settled and he was discharged at his own request nine weeks later. He was then in good condition, having gained a stone in weight, but cough was still present and his sputum remained positive for tubercle bacilli. There was still a little fluid in his right pleural space, but this gradually disappeared over the next three months.

He continued to receive pneumothorax refills as an out-patient as it was felt that small cavitation persisted in the right upper lobe, his pneumothorax being finally abandoned on 21st December 1945 when, on screening him, it was noticed that an effusion had again occurred in the right pleural space.

The remaining air soon became absorbed but the fluid increased in amount and, on 24th May 1946, 32 ounces of chocolate-coloured fluid were aspirated. Smears showed numerous lymphocytes and red blood cells, but tubercle bacilli were not seen, and culture for pyogenic organisms was negative. Amounts of similar fluid varying from 14 to 22 ounces were withdrawn, at first at three-weekly intervals, and latterly at intervals of three months.

On 9th July 1947 when an X-ray film showed the presence of a dense right-sided pleural effusion, 16 oz. of chocolate-coloured fluid



were aspirated. Smears of this fluid did not contain tubercle bacilli but showed numerous degenerated cells, some of which contained fat globules, numerous polymorpho-nuclear leucocytes and clumps of cholesterol crystals.

The cholesterol content of the fluid was 300 mgm. per cent., the blood cholesterol level being 160 mgm. per cent. The protein content was 12 gm. per cent. (albumin 9.2, globulin 2.8) as against the plasma proteins of 7 gm. per cent. (albumin 4.2, globulin 2.55, fibrin 0.25).

On 15th October 1947, 12 ozs. of similar fluid were withdrawn and numerous cholesterol crystals were again seen; the cholesterol content was 450 mgm. per cent., the blood level being 180 mgm. per cent. The fluid had a high specific gravity (1073) with a total protein content of 21 gm. per cent. (albumin 17.4, globulin 3.6). The plasma protein amounted to 7.55 gm. per cent. (albumin 5.8, globulin 1.75). The fluid had a characteristic sheen and a specimen, transferred to a test-tube and kept in the refrigerator, showed a white band near the surface of the fluid, composed of masses of cholesterol crystals.

Tubercle bacilli were not seen on direct examination or after culture on Lowenstein Jensen medium. Culture for pyogenic organisms was negative. There was no abnormality of his blood or urine and his Wassermann was negative.

Since the onset of the effusion he has remained well and in full employment with the Observer Corps. He has been afebrile, his B.S.R. has varied between 5 and 10, and such sputum as he occasionally managed to produce has been negative for tubercle bacilli on direct examination. The only complaint he has had is that of an occasional dragging pain in the right side of his chest.

A recent X-ray film shows the same dense pleural thickening and effusion on the right side, and below it, much nodular and calcified shadowing which has the appearance of healed disease. There is marked shrinkage of the right side of the chest with traction on the trachea and mediastinum to that side.

**TREATMENT.**—As regards treatment of the condition, one should strike the happy mean between too frequent aspirations and complete lack of interference. The patient usually has little in the way of complaints relative to the effusion, but should pressure symptoms develop, aspiration should be carried out. The pleura is usually so thickened that repeated aspiration will not cause elimination of the pleural space, but might instead lead to secondary infection of the fluid. On the other hand, if no attempt at periodic aspiration is made—*e.g.* every 3 to 4 months but depending on the amount of fluid present, and the rate at which it collects—the possible complication of broncho-pleural fistula, one case of which has been reported by Coyon, must be borne in mind.

**DISCUSSION.**—Attempts to postulate the cause of such effusions are hampered by the fact that little is known of the function of cholesterol in the body. It is biochemically related to the steroid hormones of

the ovary, testicle and adrenal cortex, and in this respect, it is of interest to note that almost all of the cases so far recorded have occurred in middle-aged adults. The presence of cholesterol crystals in the effusions, however, does not seem to be associated with a general upset of cholesterol metabolism as the blood level in such cases is usually within normal limits

Erwin suggests that there is a protracted exudation containing cholesterol derived from the blood stream, and that the marked pleural thickening which is usually present prevents a free interplay of the constituents. This does not explain, however, why cholesterol crystal formation should occur in only a very small percentage of chronic effusions, in the majority of which the above conditions exist.

Desbordes and his associates consider that the albumin-globulin ratio of the fluid plays an important part in the presence or otherwise of the crystals. They state that, as the albumin-globulin ratio falls below one, cholesterol is precipitated, while with a ratio greater than one, the cholesterol remains in solution. In the case just described, however, the albumin and globulin values were 17.4 and 3.6 gm. per cent. respectively, giving a ratio of 4.8, yet crystals were present. Alteration of this ratio *in vitro*, to 2 did not give rise to any change in the numbers of cholesterol crystals seen microscopically.

Durham and Diamond suggest that, if the effusion is tuberculous in nature, the cholesterol crystals may result from destruction of the tubercle bacillus with alteration in its lipoid constituent. This might also account for the rarity with which tubercle bacilli are recovered from such fluids.

The following theory seems a simpler one:—Some fluids, on coming into contact with cholesterol, tend to precipitate any cholesterol which they contain, and it may be that solid cholesterol from a degenerated or caseous focus in the pleura or sub-pleural zone may cause such a change in a pleural effusion which may already contain a high cholesterol content due to prolonged exudation with pleural thickening. Once this had been brought about, cholesterol crystals remaining after incomplete evacuation of the effusion could cause perpetuation of the process.

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## NOTE

NOTICE is hereby given that, at an Extraordinary meeting of the Royal College of Surgeons of Edinburgh held on 24th March 1948, the Laws relating to the Fellowship by Examination were amended as follows:—*Part I.* A written paper and an oral examination in Anatomy and Physiology.

A written paper and an oral examination in Pathology and Bacteriology.  
*Part II.* On the Principles and Practice of Surgery and on an optional subject to be chosen by the candidate from among the following:—(1) Surgical Pathology and Operative Surgery, (2) Laryngology, Otology and Rhinology, (3) Obstetrics and Gynaecology and (4) Ophthalmology.

The new Laws come into operation on 1st January 1949.

Candidates who have appeared for the Fellowship Examination on or before 15th March 1948 will be allowed to reappear for the examination at any time under the conditions set forth in the Laws at present in operation.

Candidates who appear for the examination for the first time on 28th June 1948 and are unsuccessful will have an opportunity of reappearing for the examination on 1st October 1948 under the existing Laws, but thereafter, if necessary, they must reappear under the new Laws.

Candidates who appear for the examination for the first time on 1st October 1948 and are unsuccessful must thereafter appear under the new Laws.

In the name and by the Authority of the College.

K. PATERSON BROWN, M.B., F.R.C.S.ED.

*Secretary*

18 Nicolson Street, Edinburgh

## BOOKS RECEIVED

- |  |               |
|--|---------------|
| BANKOFF, GEORGE, M.D., D.CH., F.R.F.P.S., F.R.C.S.E. The Practice of Local Anæsthesia. Third Edition . . . . . (Staples Press)   | 30s.          |
| BAILEY, HAMILTON, F.R.C.S.(ENG.), F.A.C.S., F.I.C.S., F.R.S.E. Emergency Surgery. Part I. Sixth Edition (John Wright & Sons Ltd., Bristol)   | 21s. net.     |
| BIDDLE, W. EARL, M.D., and SICKEL, MILDRED VAN, B.S., R.N. Introduction to Psychiatry. Second Edition . . . . . (W. B. Saunders Company, London)   | 14s.          |
| CAMERON, NORMAN, M.D., PH.D. The Psychology of Behavior Disorders. (Houghton Mifflin Company, New York)  | 25s. net.     |
| COLE, LESLIE, M.A., M.D.(CAMB.), F.R.C.P. Dietetics in General Practice. Second Edition . . . . . (Staples Press, London)  | 8s. 6d. net.  |
| CROSSEN, HARRY STURGEON, M.D., and CROSSEN, ROBERT JAMES, M.D. Operative Gynecology. Sixth Edition . . . . . (Henry Kimpton, London)   | 75s. net.     |
| DEVINE, SIR HUGH, M.S.(MELB.), HON. F.R.C.S.(ENG.), F.R.A.C.S., F.A.C.S., and DEVINE, JOHN, M.S.(MELB.), F.R.C.S.(ENG.), F.R.A.C.S., F.A.C.S. The Surgery of the Colon and Rectum (John Wright & Sons Ltd., Bristol) | 52s. 6d. net. |
| EDWARDS, HAROLD C., C.B.E., M.S., F.R.C.S. Recent Advances in Surgery. Third Edition . . . . . (J. & A. Churchill Ltd., London)  | 24s.          |
| GOULD, SIR ALFRED PEARCE, K.C.V.O., C.B.E., M.S., F.R.C.S., and WAKELEY, SIR CECIL, K.B.E., C.B., D.S.C., F.R.C.S., F.A.C.S. Elements of Surgical Diagnosis. Ninth Edition . . . . . (Cassell & Co. Ltd., London)    | 15s. net.     |
| HUNT, ELIZABETH, B.A., M.D., CH.B.(LIVERPOOL). Diseases Affecting the Vulva. Third Edition Revised . . . . . (Henry Kimpton, London)   | 25s. net.     |
| JENNINGS, W. A., B.SC., A.INST.P., and RUSS, S., C.B.E., D.S.C., F.INST.P. Radon: Its Technique and Use. (Published for The Middlesex Hospital Press by John Murray, London)   | 18s. net.     |
| JOHNSTONE, R. W., C.B.E., M.A., M.D., F.R.C.S.E., M.R.C.P.E., F.R.C.O.G., F.R.S.E. A Text-Book of Midwifery. Thirteenth Edition. (Adam and Charles Black, London)  | 30s. net.     |

# Edinburgh Medical Journal

May 1948

## THE TREATMENT OF THYROTOXICOSIS \*

By D. M. DUNLOP, B.A., M.D., F.R.C.P.

Professor of Therapeutics, The University of Edinburgh

DURING the last four years we have treated nearly 200 cases of primary and secondary thyrotoxicosis with thiouracil. In this communication, however, we shall refer only to the results of treatment of the 149 patients treated during the first three-and-a-half years since those who were only encountered during the last six months have been observed for too short a time to permit of any useful conclusions being made from them. Of the 149 patients observed for periods of time varying from six months to three-and-a-half years, 83 were treated originally in hospital, usually for about a month, and 66 have been treated throughout as out-patients. Initial out-patient treatment for mild cases has only been started during the last two years. Previously our experience of thiouracil had been insufficient to justify the proceeding. It has only proved necessary to submit 19 of the 149 patients to thyroidectomy. We will discuss later the factors which made this necessary.

*Pharmacology.*—The broad principles of the pharmacology of anti-thyroid substances are now well known. Briefly, they produce their effect by interfering directly with the synthesis of the thyroid hormone, probably by preventing the iodination of tyrosine. In consequence an effect on the raised metabolism of thyrotoxic individuals is rapidly produced since their glands contain practically no stores of thyroxine. If a large dose of the anti-thyroid substance is continued for a sufficient time myxoedema will result, with a compensatory increased production of thyrotropic factor from the anterior pituitary, causing thyroid hyperplasia. The aim of treatment is to produce the optimal clinical effect by a high initial dosage and then to keep up that effect by an appropriate smaller maintenance dose, just as is done in the case of digitalis.

*Dosage.*—All workers are now in general agreement on the principles of dosage. The initial dose consists of 0.2 gm. thiouracil three times a day. At the end of three weeks or a month, when a significant

\* Read at a meeting of the Medico-Chirurgical Society of Edinburgh on 14th January 1948.

clinical effect has usually been brought about, this dosage can be reduced to a maintenance one—in severe cases to 0.2 gm. and in mild cases to 0.1 gm. daily. After all thyrotoxic signs and symptoms have remained in abeyance for some months a further reduction in dosage can be attempted to 0.1 gm. and finally to 0.05 gm. in the day. A return of symptoms will, of course, necessitate an appropriate increase in the dose. If after three or four months on 0.05 gm. a day there has been no sign of a return of thyrotoxicosis, a trial may be made of stopping the drug altogether; but, as we shall see, relapse is extremely common if treatment has not been continued for at least a year. We have used this scheme of dosage for four years.

*Preparations.*—It matters not whether thiouracil or methyl-thiouracil is employed. It has been claimed on entirely inadequate evidence that the latter is less toxic than the former. We have not observed any difference between the two in this respect, but as methyl thiouracil is slightly cheaper it is the preferable preparation. It may well be that the new propyl thiouracil will turn out to be much less toxic than either of the older preparations and may be the drug of choice in the future. So far we have had no experience of its use.

TABLE I

	Average Blood Cholesterol in mg. per cent. 28 Cases.	Average B.M.R. 56 Cases.	Average Weight in Kilos. 83 Cases.
Before treatment . . . . .	150	+51	54.0
After one month's treatment in hospital	218	+14	57.5

### CLINICAL EFFECTS

The effects of thiouracil in thyrotoxicosis are on the whole fairly precise and predictable. For a few days no result is observed, but at the end of a week some subjective improvement occurs—the sweating and flushing of the skin being usually the first symptoms to be ameliorated. Thereafter all the thyrotoxic signs and symptoms steadily improve, the improvement being significant in three or four weeks' time and maximal in two or three months, when even initially severely ill patients are usually fit to return to work. The objective and measurable signs of thyrotoxicosis parallel the subjective sensations of the patient in their improvement.

After a latent period of about ten days a fall in the B.M.R. becomes noticeable which usually reaches significant proportions in three weeks to a month's time, after which the initial dose of thiouracil can be reduced to a maintenance one. The blood cholesterol concentration and the weight rise as the B.M.R. falls, becoming almost mirror images of the latter.

*The Blood Cholesterol.*—The blood cholesterol concentration is low in untreated hyperthyroidism just as it is high in myxoedema. Taking the average of a number of cases it rises under the influence of thiouracil, but this reading does not constitute a reliable yard-stick for the control of treatment, since in individual patients there is often little correlation between the blood cholesterol concentration and the progress of the case. We therefore abandoned this observation as a routine test after the experience of our first 28 cases.

*The B.M.R.*—The B.M.R. is a clinical test which is often endowed with the greatest potentialities by those with little experience of it. Actually it is a procedure which lacks universality of application in ordinary practice, and is certainly not one which should be conducted on out-patients without admitting them to hospital for a night or

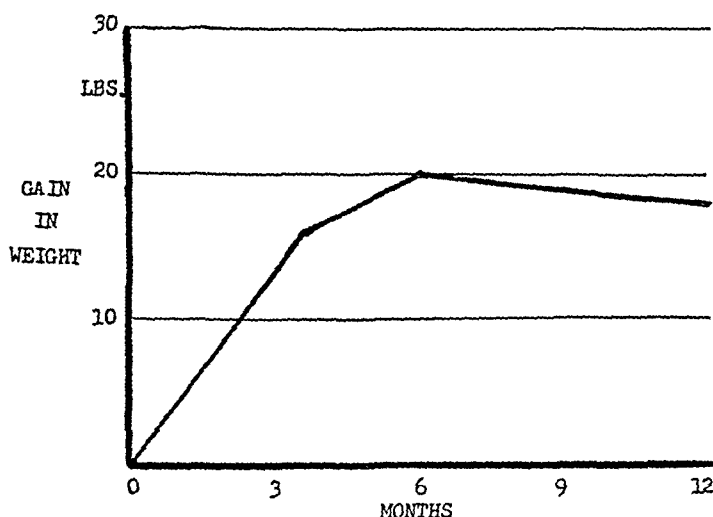


FIG.—Average Gain in Weight of 83 Patients treated with Thiouracil for One Year.

more if accurate results are to be obtained. Even in hospital many patients become over-anxious about their B.M.R. readings and in consequence artificially high estimations are obtained. The effect of thiouracil on the metabolism is on the whole so precise as to make B.M.R. readings superfluous. After our observations on the first 56 cases we abandoned this as a routine observation also and have come to rely on our ordinary clinical impressions far more than on blood cholesterol and B.M.R. readings.

*Weight.*—Particularly, we rely on the weight as a prognostic sign. This, on the average, increases steadily during the first month of treatment. The average gain in weight of the 83 patients treated for a month in hospital was  $3\frac{1}{2}$  kg., or over half-a-stone; but if these are followed up for a year it will be seen from Chart I that the average gain in weight reaches the rather astounding total of 20 lb., a somewhat embarrassing attribute to treatment in those days of coupons,

and an effect which may even be a drawback to thiouracil treatment as it may be to thyroidectomy in patients who are not originally under weight. One of our patients actually gained over 5 stone in weight as the result of treatment with thiouracil.

*Tachycardia.*—Thiouracil does not act uniformly on all the signs of thyrotoxicosis and the last to show improvement is, on the whole, the associated tachycardia and high pulse pressure. When a marked degree of tachycardia exists its control is often delayed long after the B.M.R. has fallen to normal and the weight and other signs and symptoms have greatly improved. The only unfavourable features at all commonly encountered in our follow-up clinics have been some persistent tachycardia and raised pulse pressure in a small proportion of cases.

*In summary*, we believe that thiouracil ultimately exerts an effect on the blood cholesterol concentration, the B.M.R. and weight, entirely

TABLE II  
*Seven Cases of Thyrotoxic Fibrillation*

Case.	Thiouracil.	Thiouracil + Quinidine.	Thyroidectomy.	Thyroidectomy + Quinidine.
1	+ in 24 days			
2	+ in 28 days			
3	— after 10 days	+ in 1 day		
4	— after 6 weeks	+ in 2 days		
5	— after 5 weeks		—	+ in 2 days
6	— after 2 months		—	+ in 3 days
7	— after 3 months	— after 4 days	—	— after 5 days

+ = Return to normal rhythm.

comparable to successful thyroidectomy. Thyroidectomy produces a much more dramatic immediate effect on tachycardia than thiouracil and the ultimate beneficial effect may also be superior—an argument in favour of its use in secondary nodular goitre.

*Auricular Fibrillation.*—In some cases the auricular fibrillation due to thyrotoxicosis returns spontaneously to normal rhythm under the influence of thiouracil just as normal rhythm may occur spontaneously after thyroidectomy. In a number of cases, however, the fibrillation persists in spite of satisfactory control of the other features of hyperthyroidism by thiouracil, just as it may persist after thyroidectomy, and quinidine treatment may be necessary to restore the rhythm to normal. The experience of the 7 cases shown in Table II is quite inadequate to allow any comparison to be made between thiouracil and thyroidectomy in their respective effectiveness in restoring fibrillation to normal rhythm. The literature on the subject suggests that thyroidectomy is the more effective of the two, but there is almost no reference in it to the combined use of thiouracil and

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quinidine, whereas quinidine was frequently employed following thyroidectomy.

*Glycosuria*.—The mild diabetic state so commonly associated with thyrotoxicosis may often be cured by thiouracil just as it may be cured by thyroidectomy. There are, of course, other thyrotoxic cases complicated by severe diabetes, and such diabetes is not cured, though it may be ameliorated, both by thiouracil and by thyroidectomy.

*Exophthalmus*.—In 149 cases studied, thiouracil did not materially affect the degree of exophthalmus present. Lid-retraction disappeared in a proportion of patients after prolonged treatment, but we have little doubt that lid retraction shows on the average a greater decline after thyroidectomy than after treatment with thiouracil.

*Size of Goitre*.—On the whole also, thiouracil in the dosage used does not greatly diminish the size of the goitre. When this is large and disfiguring it constitutes a definite disadvantage to thiouracil treatment, particularly if there is any tendency to pressure symptoms. On the other hand, when the goitre is small it is less cosmetically disfiguring than some of the scars which result from its surgical removal. Slight fluctuations in the size of the goitre under thiouracil treatment may be noted from week to week and month to month. A fairly constant feature is the increase in the size of the gland coincident with the menstrual period and a recession after it. Almost invariably the goitre becomes softer in contrast to the firmer gland produced by iodine therapy. Occasionally the gland becomes definitely smaller, and when the thyrotoxic tendency has been abolished by thiouracil, and it has been possible to give up the use of the drug altogether, the size of the gland may diminish very materially.

Theoretically it would seem that if the pituitary is stimulated by *over-dosage* with thiouracil to produce excess of thyrotropic hormone, an increase in the size of the goitre will occur similar to the hyperplasia produced by goitrogenic substances in experimental animals. This certainly occurs in practice when a patient is overdosed with thiouracil, and we have had 4 cases ( $2\frac{1}{3}$  per cent.) in which a greater or less degree of myxœdema and thyroid hyperplasia has occurred. In the literature the incidence of myxœdema after thyroidectomy and with thiouracil is put at about 4 per cent. in each case, but myxœdema caused by treatment with thiouracil is temporary, whereas after thyroidectomy it is permanent.

*Toxic Effects*.—The toxic changes which we have encountered as the result of thiouracil are shown in Table III. Sixteen (11 per cent.) of the patients showed a greater or less degree of intolerance to the drug, and 9 of them (6 per cent.) developed sufficiently severe toxic symptoms to require the abandonment of treatment. In this series there has, however, been no mortality either from the toxic effects of thiouracil or from uncontrolled thyrotoxicosis.

A study of the literature suggests that the incidence of toxic manifestations is about 13 per cent., being sufficiently severe in over half of

usually in the non-hospital class—who will dislike the idea of continuing drug treatment for a long period of time without the certainty of permanent cure. They develop a complex about their goitre and are anxious to have it removed once and for all. Provided the case is not one of mild primary thyrotoxicosis in a young girl, the patient is entitled to some choice in the matter after the advantages and disadvantages of both methods of treatment have been thoroughly explained.

We believe that thiouracil is the treatment of choice in young people with primary thyrotoxicosis, provided of course that the goitre is not very large and unsightly. The idea of radical surgical interference with the endocrine system in such cases is repugnant if it can be avoided, and we know that some of them, particularly mild cases, will subside spontaneously without any treatment at all, and many more will subside with wise psychological guidance and with the help of thiouracil. The risks of thiouracil treatment in such cases are certainly not more than the operative risks of thyroidectomy and much less than the risks of operation in the hands of surgeons unpractised in the great art of goitre surgery. If the primary thyrotoxic case develops intolerance to thiouracil, or if the results of treatment are unsatisfactory in any way, surgery is always a second line of defence.

All cases of recurrent thyrotoxicosis following thyroidectomy should be treated with thiouracil, since the results of further operation are often unsatisfactory in such cases.

Lastly, really old thyrotoxic patients often with degenerative disease, are probably better treated conservatively with thiouracil than by means of thyroidectomy.

We feel much less certain as to the wisdom of treating cases of secondary or nodular goitre in middle-aged patients with thiouracil. Many of them improve greatly as the result of such treatment, but there is much more justification for thyroidectomy in such circumstances. Radical interference with the endocrine system is less objectionable in middle-aged people, and it may well be that thyroidectomy exercises a more beneficent influence on the characteristic circulatory disorders of such patients than does thiouracil.

## THE SURGICAL TREATMENT OF THYROTOXICOSIS \*

By K. PATERSON BROWN, M.B., CH.B., F.R.C.S.

Surgeon, The Royal Infirmary, Edinburgh

IN his paper Professor Dunlop has shown what excellent results can be obtained with thiouracil, but he has not claimed that this drug is the complete answer to the thyrotoxic problem. Similarly, I make no claim that surgery is the perfect treatment. Physician and surgeon alike are trying to find some common ground from which they may make a further advance.

The introduction of thiouracil in 1943 opened a new era in the treatment of thyrotoxicosis. In medical schools throughout the world this new form of treatment has had a profound effect upon the surgical treatment of this disease, and in Edinburgh the effect has been particularly striking. Whereas before the introduction of thiouracil almost every patient was dealt with by surgery, after its introduction there was a rapid swing-over to medical treatment. This is best illustrated by a graph showing the number of patients operated upon in the Royal Infirmary between the years 1936 and 1946. The peak year was 1939, and thereafter there was a gradual fall until 1943, probably associated with the population changes in the war years. With the introduction of thiouracil in 1943 the number of thyroidectomies in 1944 fell to 61 and in 1945 to 34. During 1946 the number rose to 48, and in 1947 the curve rises again. I cannot give you the total figures for 1947, but I have operated upon 46 patients, and therefore the total for all surgical charges must be considerably higher than in the previous year. This rise suggests that the pendulum had swung too far towards medicine, and that it is now approaching a more even balance as between medicine and surgery.

I believe that it would be correct to say that the reduction in the number of thyroidectomies in Edinburgh is more striking than in some other centres because thiouracil has been used with varying degrees of enthusiasm in different centres and in some thyroidectomy is still a very common operation. Its early use in Edinburgh, with undoubted benefit to thyrotoxic patients, is an indication of the natural desire of our medical colleagues to investigate, under carefully controlled conditions, a new drug which might eliminate the need for an operation which the surgeon readily admits is not a scientific procedure. How carefully this question has been investigated Professor Dunlop has demonstrated, but he has also shown that there is still a place for the surgeon.

As I have already indicated, for the past few years that place has

\* Read at a meeting of the Medico-Chirurgical Society of Edinburgh on 14th January 1948.

been rather a lowly one, and no single surgeon has had an opportunity of operating upon many patients. I have only carried out 94 thyroidectomies for thyrotoxicosis since 1944. I propose to refer only to those carried out since 1945, a total of 74, as during 1944 the patients that I saw had often had incomplete thiouracil treatment and could not be fairly assessed as thiouracil failures.

I must explain the method adopted in the selection of patients for surgical treatment. When we are consulted by a patient with thyrotoxicosis, that patient is referred to a physician so that every patient who is operated upon comes to us at the request of our medical colleagues who may or may not have considered thiouracil desirable.

To begin with, thiouracil was used in place of iodine for the pre-operative preparation, but it soon became evident that it was unsuitable for this purpose. The thyroid gland became soft, friable, and very vascular, greatly increasing the difficulties of the operation. In addition, the post-operative period tended to be more stormy, but this may well have been due to the more prolonged operation rather than to the drug itself.

The second phase saw thiouracil and iodine being used together, the former being continued up to the time of operation and sometimes post-operatively also. This method I consider to be unsatisfactory. The full value of the iodine is not obtained and there would appear to be a definite increase in the incidence of infection, a complication that is most uncommon under ordinary circumstances.

In spite of these drawbacks, I feel certain that there is a place for thiouracil in the preparation of patients for thyroidectomy. The drug should, however, be stopped ten or twelve days before operation, that is, when the iodine administration is commenced. The following composite graphs of pulse readings during and after operation in a series of patients prepared with thiouracil and iodine, and a second series prepared with iodine alone, demonstrate a fact which I have become convinced of from my clinical experience. These groups of patients were so far as possible comparable in that only those with severe thyrotoxic symptoms were included.

The upper pulse curve shows the typical graph in a patient prepared with iodine, a rapid rise during tracheal intubation, then a fall with a further rise after the incision, reaching its maximum with the mobilisation of the thyroid and thereafter a progressive fall. Compare this with the lower curve obtained when thiouracil followed by iodine have been employed. The difference is, I think, striking and important. A similar state of affairs is seen in the pulse readings during the post-operative period.

#### THE INDICATIONS FOR THYROIDECTOMY

*Primary Toxic Goitre.*—In the past, surgery has given excellent results in a high percentage of cases, but there remained a small group

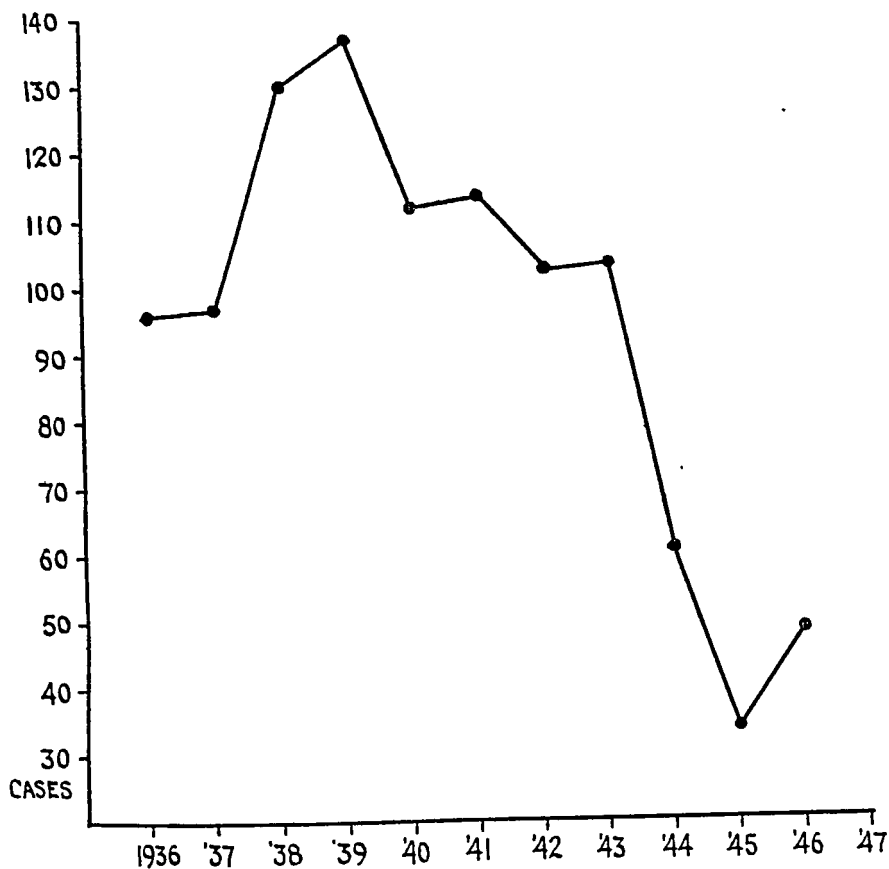


FIG. 1.

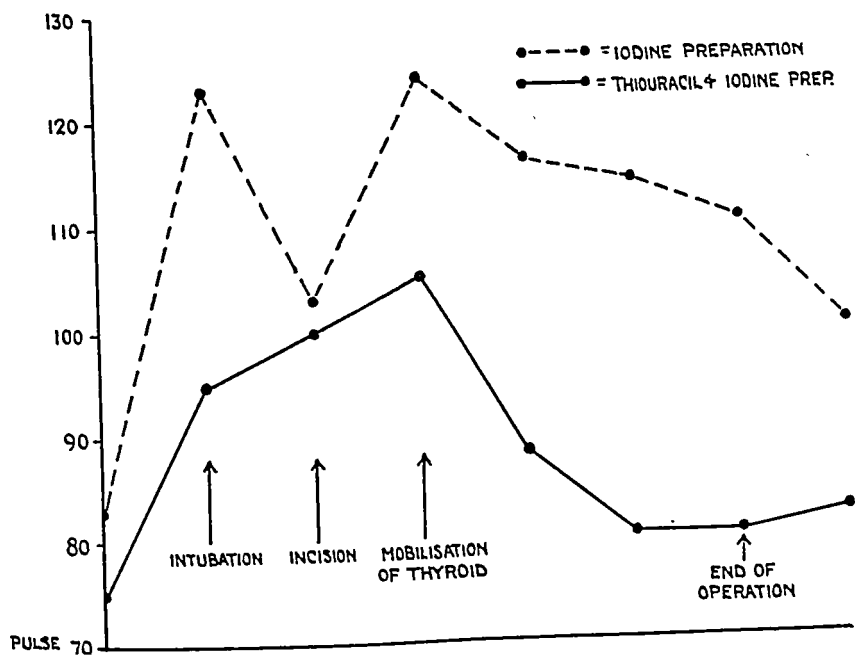


FIG. 2.

who were only partially relieved or failed to derive benefit. There were also a small number who, apparently cured, later developed symptoms associated with hyperplasia of the thyroid. In my experience these failures are almost invariably met with in females. There are few more satisfactory operations than thyroidectomy on a male patient with primary thyrotoxicosis.

I agree with Professor Dunlop that a patient, and especially a young patient suffering from primary toxic goitre, should be given the chance of cure or control by thiouracil, but as he has said, a certain number of such patients will require operation later. I consider that the following are the indications for operation :—

- (1) If thiouracil fails to control the symptoms.
- (2) If thiouracil causes some serious complication requiring withdrawal of the drug.
- (3) If thiouracil causes excessive enlargement of the thyroid with a tendency to pressure symptoms.
- (4) The desire of the patient.
- (5) Inability to keep the patient under adequate control during the treatment or if the patient fails to co-operate.

*Secondary Toxic Goitre.*—From this group I exclude for the moment those patients with cardiac lesions. I think it will be agreed by physicians and surgeons alike that the operative treatment of secondary thyrotoxicosis has given outstanding results. I have yet to see an example of true recurrent thyrotoxicosis occurring in this type of case provided that a subtotal thyroidectomy has been carried out.

I am not convinced that thiouracil is the best treatment for secondary toxic goitre. In my opinion these patients should be operated upon. In this connection it is interesting to note that, whereas before the introduction of thiouracil 24 per cent. of all our patients treated by thyroidectomy suffered from secondary toxic goitre, since 1944 the percentage has risen to 43 per cent., indicating that the results of thiouracil treatment in secondary thyrotoxicosis have been less satisfactory than in the primary group.

Some of these patients have pressure as well as toxic symptoms and such patients ought not to be given thiouracil ; this is especially important if there is any retrosternal prolongation of the gland.

Operation gives excellent results and these patients do not relapse with later cardiovascular breakdown. Has sufficient time elapsed since the introduction of thiouracil for us to be equally certain about the results of medical measures ? If the activity of the thyroid is completely controlled, well and good, but if the treatment only achieves partial control, and this I believe to be very common, the patient's symptoms will doubtless be improved, but may time not show that cardiac changes will supervene ? I do not think that that question can yet be answered with certainty.

There is one other matter to which I must refer, although the answer



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Fig. 1



Fig. 2

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Fig. 3

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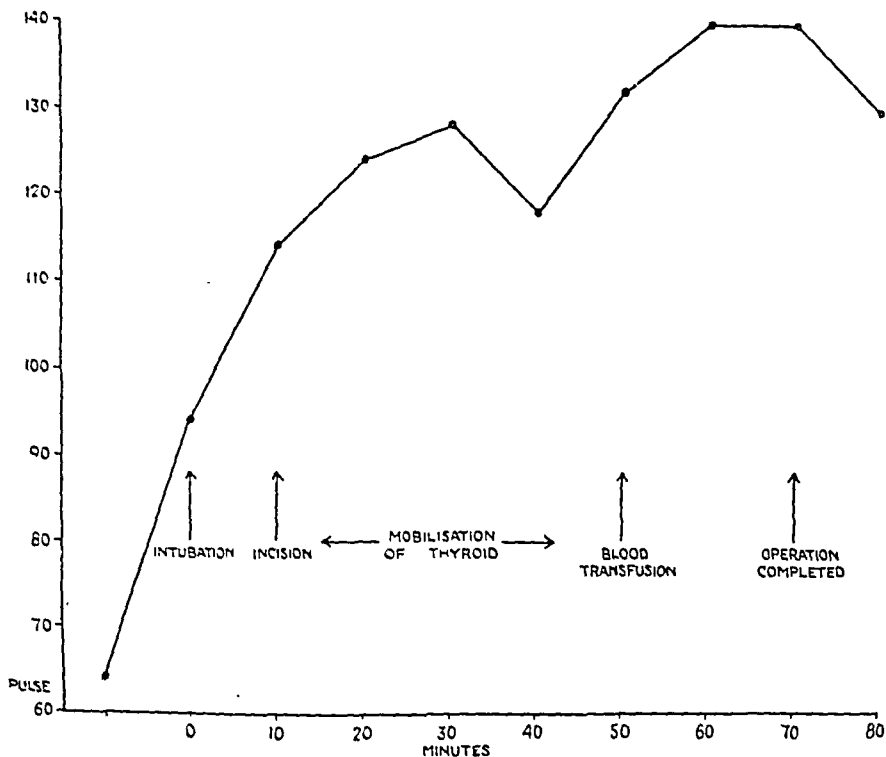


FIG. 3.

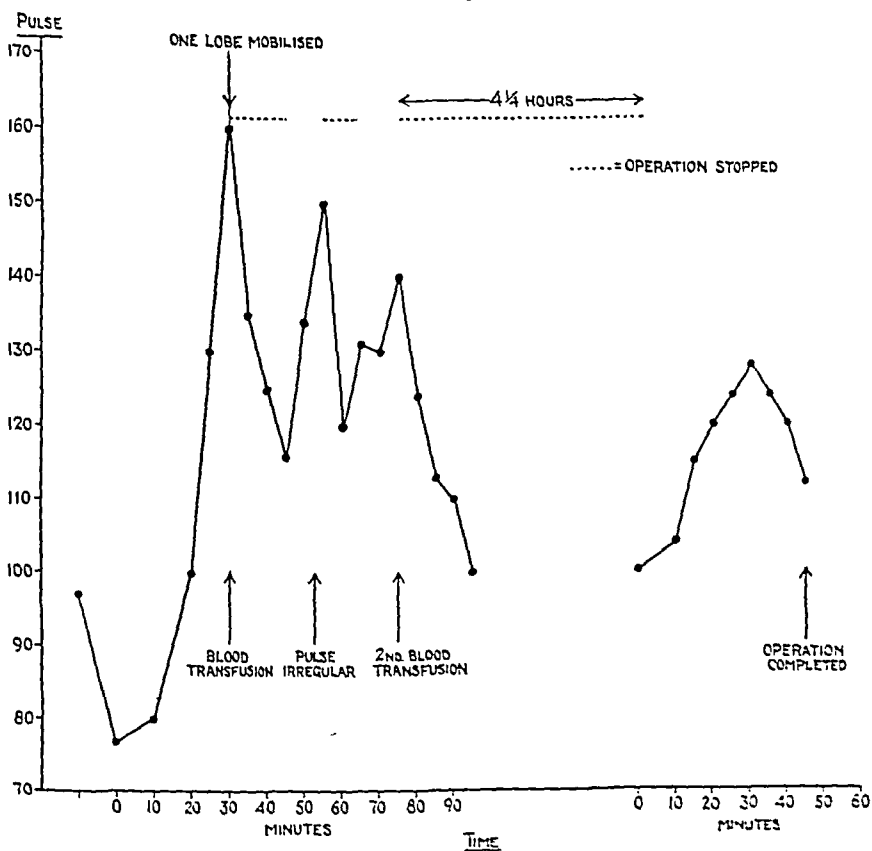


FIG. 4.

is not yet forthcoming. We see with distressing frequency patients who suffer from malignant disease of the thyroid. This develops mainly in the nodular type of gland and more often in the simple than the toxic thyroid. Is it not possible that time may show that malignant disease may develop in a secondary toxic thyroid continually under the influence of thiouracil? This may be a theoretical danger, but none the less it requires consideration.

*Secondary Toxic Goitre with Cardiac Manifestations.*—Patients in this group present a serious problem to physicians and surgeons, and unless the patient comes under treatment before gross cardiac breakdown has occurred, a truly satisfactory result cannot be obtained. We have all seen dramatic results in this type of case as a result of thyroidectomy, patients with gross cardiac irregularity and quite unable to work, restored to a normal rhythm and able to resume full employment. Such a happy result is by no means always attained, and the risks of operation are necessarily greater. In this series of 74 patients, 9 were referred to me by the physicians because of cardiac breakdown. All recovered but all were not cured. Many of these patients have cardiac changes which are irreversible and only partial improvement can be achieved. It is the early cardiac case that the surgeon hopes for, such patients can be adequately dealt with by surgery and the mortality is low.

*Recurrent Thyrotoxicosis.*—I have already referred to this group of patients whose symptoms recur after an apparently successful thyroidectomy. We know that a second operation often but not always results in a cure, but it is fraught with difficulty and the risks of damage to parathyroid glands or to recurrent laryngeal nerves are much increased. I believe that such patients should be referred to the physician for thiouracil treatment, and only if that fails should a second operation be carried out.

It is not my intention to deal with the details of operative technique, but I would like to refer to two matters. It is my custom to have the pulse-rate charted at five-minute intervals throughout the operation. The graph so obtained gives an accurate guide to the state of the patient. I believe that the pulse curve is more important than the actual rate. I have already shown you what we consider is the normal operation pulse curve which shows a gradual fall after mobilisation of the gland, so that the pulse reading at the end of the operation is approximately the same as at its commencement. If, however, the pulse-rate persistently rises after mobilisation of the gland is completed, that is a sign that all is not well with the patient, and the operation must be rapidly terminated or other methods adopted. This point is illustrated in the accompanying charts which raise a matter of the very greatest importance, and one which so far as I am aware has not been stressed before. In this series of thyroidectomies I have encountered three patients suffering from primary thyrotoxicosis, all of whom had been uncontrolled by thiouracil. In each case the thiouracil had been

administered over long periods and the thyroid was markedly enlarged. I consider this combination of findings as a danger signal. Pre-operative iodine controlled the symptoms, rendered the thyroid firmer in consistence, but in all three patients bleeding during operation was very severe and urgent blood transfusion was required. I believe that no patient in this category should be operated upon without all facilities for immediate blood transfusion being available.

There is one other point in connection with the operation to which I would like to refer. For the past three months I have been using an oxidised cellulose gauze for the control of that annoying and sometimes troublesome blood ooze which occurs from the divided thyroid even after all vessels have been ligated and the thyroid stumps sutured. This gauze is laid over both thyroid remnants and the trachea, and it produces almost instantaneous hæmostasis. Its use has been of immense assistance to me, and I have now abandoned drainage of the neck. The gauze is completely absorbed, appears to produce no reaction, and no complications have been met with since I commenced to use it.

*The Complications of Thyroidectomy.*—Tetany is a rare complication, and I believe that it is better not to make a practice of trying to demonstrate the parathyroid glands during operation. In this series I have had one case of tetany which was rapidly controlled by treatment, and four months later the patient was well and the signs of tetany had disappeared.

Bilateral recurrent nerve damage has not occurred, but in the last hundred operations three patients developed symptoms pointing to unilateral nerve damage and confirmed by a laryngologist. Two have recovered completely, but in the third recovery is still incomplete.

By far the most important complication is hæmorrhage. Its importance lies in the fact that it causes sudden and serious dyspnœa, and death may result if treatment is not instituted promptly. I have met with this complication on five occasions, although it has not occurred in the series under review. It has always been encountered in patients with secondary thyrotoxicosis, always about five or six hours after operation, and always the result of a general ooze of blood and not from a single bleeding point. In every case the wound was rapidly reopened, the clot evacuated and the wound loosely packed. Later the wound was resutured and all the patients made a satisfactory recovery.

*Mortality.*—There have been no deaths in this series of 74 patients, and my mortality for all thyroidectomies, primary, secondary and cardiac cases, is 1·6 per cent.

In conclusion may I say that whatever the future may bring in the shape of new drugs for the treatment of thyrotoxicosis, at the present time physician and surgeon must continue and are continuing that close co-operation which has proved so pleasant and successful in the past.

## DISCUSSION

*Dr W. A. Alexander*, opening the discussion, said that some sixty thiouracil-treated patients had been reviewed for him by Dr J. B. Borthwick, and that he had had to regard the long-term results as somewhat disappointing. This was due partly, he now considered, to inadequate duration of treatment and in some cases to insufficient dosage. One of the series had died, while receiving a maintenance dose, from what seemed to be a thyrotoxic crisis, but there were complications in the case. Apart from this, he had had only one alarming experience. This was in the case of a female aged thirty-eight who had had a thyroidectomy performed in 1941 and who had relapsed and been given thiouracil elsewhere for a few months in 1945. She was admitted to his ward in August of last year. There was considerable hyperplasia of the residue of the gland, and very positive, though not severe, thyrotoxicosis. The leucocyte count was regarded as adequate (4500) and 0.6 gm. daily of thiouracil was given. On the twelfth day it was reported that the count had dropped to 2000, but a second count was nearer 3000. The drug was not stopped but reduced to 0.2 gm. daily. The following day, however, the temperature rose and she became alarmingly ill, presenting the picture of agranulocytic angina. The white cells fell to 1000 with not a single granular cell in the film. With the help of penicillin, pyridoxin and blood transfusion she eventually made a good recovery. An interesting point was that, at a stage when he was despairing of the patient's recovery, he was given a good prognosis by Dr J. R. Clark as a result of examination of the bone-marrow. Although there were no neutrophils in the blood, it was clear that their precursors in the marrow were still surviving.

Dr Alexander was interested to hear of the high proportion of cases treated by Professor Dunlop as out-patients. Hitherto he had insisted on the patient being admitted to hospital for the initiation of treatment, partly because he had regarded rest as a desirable part of the scheme. He was prepared, however, to accept that this was not really necessary, though he deprecated desultory treatment with thiouracil in outside practice.

He agreed with Mr Paterson Brown that, when operation was indicated, the ideal preparation was to administer thiouracil for a limited time, until what benefit was possible had accrued, and then to stop the thiouracil and give iodine for ten to fourteen days.

It was unfortunate that neither thiouracil nor operation could be guaranteed to have any effect on the ocular features of thyrotoxicosis.

There was, of course, no doubt of the great advance in the management of thyrotoxicosis marked by the introduction of thiouracil, especially in primary cases, but he did not feel quite so enthusiastic over its permanent value in the working woman or busy housewife, and a higher proportion of his patients had gone on to operation than in Professor Dunlop's series.

*Mr Graham* said it was highly important that a new drug such as thiouracil should be carefully studied in all its aspects. Professor Dunlop was to be congratulated on the results of his observations. He was sure that no more thorough investigation had been recorded in this country. There should be no rivalry between the physician and the surgeon in such an investigation, and Mr Paterson Brown had shown in his remarks that the closest collaboration had been maintained throughout. There is still some doubt as to the proportion of cases of toxic goitre which should be treated surgically. We know the results

of operation before thiouracil, and Mr Paterson Brown's operation mortality rate of 1.6 per cent. could scarcely have been improved on, considering the serious nature of many of the cases.

Most of the cases treated by thiouracil, which Mr Graham had operated on, were cases in which the treatment had failed because of intolerance, toxicity, or from the lack of response to the drug. While we know the results of medical treatment of thiouracil, as shown by Professor Dunlop's figures, we are not yet in a position to compare these with the results of a long series of cases deliberately prepared for operation with thiouracil and iodine. There is no doubt that the risks of operation are still further reduced by preparation in this way.

Mr Graham mentioned that in a series of 243 cases treated by operation before the days of thiouracil, there was a recurrence of symptoms in only six of the cases. He did not know what the recurrence rate would be after a prolonged course of thiouracil. If the risks of operation could be reduced to a level comparable to that of medical treatment, that would be an argument in favour of operation, as the patient would be restored to health and relieved from medical control more quickly.

Mr Paterson Brown had recommended that operation should be preferred to medical treatment in cases of secondary toxic goitre, and Mr Graham supported this view. Cases of secondary toxic goitre never have a spontaneous remission of symptoms, as is sometimes seen in primary cases. If an adequate operation is done, recurrence of toxic symptoms does not occur, and the patient is restored to health, unless the heart has previously been permanently damaged. A further advantage of operation is that the patient is relieved of the goitre, which itself is a source of worry. Even if the symptoms were controlled with thiouracil, the nodular gland will not return to normal, and it is difficult to understand why there should not be a recurrence of symptoms at some future date when the thiouracil is withheld.

Mr Graham said that the Society was greatly indebted to Professor Dunlop and Mr Paterson Brown for their contributions to this subject. Although the last word had not yet been said, they had greatly advanced our knowledge of toxic goitre and its treatment.

*Dr A. Rae Gilchrist* also spoke.

*Professor Dunlop* and *Mr Paterson Brown* thanked the audience for the kind reception of their papers, and replied suitably.

## PULMONARY MONILIASIS

By R. F. ROBERTSON, M.B., M.R.C.P. Ed.

Clinical Tutor in Medicine, Royal Infirmary of Edinburgh

RECENT work by Gow Brown (1946, 1947) has stimulated clinicians to think more carefully about *monilia albicans* as a causative agent in chronic pulmonary conditions of doubtful ætiology. British literature contains scanty references to this subject in contrast to the American literature which, especially since 1931, gives the impression that monilia infection of the lungs is a relatively common condition.

The following case report illustrates the difficulties which arise in establishing a definite diagnosis when pulmonary moniliasis is suspected.

Mrs R., æt. 42, was admitted to the Royal Infirmary, Edinburgh, on 29th October 1946.

She had no important illness until 1925 when at the age of 21 she developed a severe bronchitis following a coryza. Thereafter she was subject to attacks of bronchial asthma for which she was investigated and treated several times in hospital. Case notes made at these times indicate that the asthma was thought to be secondary to chronic bronchitis. X-ray and sputum examinations were essentially negative.

In 1942 the frequency of the asthmatic attacks had lessened, but cough was worse and accompanied by copious muco-purulent sputum. Since she had recently been in contact with a case of tuberculous pleurisy, she was referred to the Tuberculosis Dispensary for investigation. X-ray of the chest showed fibrotic lesions in both upper lobes with cavitation on the right side. Pulmonary tuberculosis was suspected but, in the course of two years' constant observation, tubercle bacilli were never found in the sputum despite repeated direct examinations, cultures and guinea-pig inoculations. It was found on the contrary that *monilia albicans* was constantly present. She was eventually discharged from the Dispensary as being non-tuberculous.

In July 1946, three months before her final admission to hospital, she became dyspnoëic on exertion with œdema of the legs and ascites. There was also profuse diarrhœa. Congestive cardiac failure secondary to lung disease was suspected and it was for treatment of this that she was admitted. Cough and copious muco-purulent sputum with occasional hæmoptysis had persisted undiminished.

On examination, she was emaciated but remarkably alert. Dyspnoëa at rest in bed was slight. There was extensive œdema of the legs and sacral region with considerable ascites. There was no finger clubbing. Examination of the chest gave signs of chronic fibrotic lesions with cavitation in both upper lobes. There was no valvular lesion of the heart. The report of a chest X-ray was as follows: "There are diffuse changes involving both lungs with fibrosis and

cavitation in the upper zones. The combined appearance strongly suggests tuberculosis in a fairly advanced state."

Pending further investigation of the sputum, a provisional diagnosis of pulmonary tuberculosis was made. Amyloid disease was also diagnosed on account of heavy albuminuria, extensive œdema, diarrhœa hypoproteinæmia, and positive Congo Red test.

**SPUTUM EXAMINATION.**—The sputum was yellow and mucopurulent.

Twelve specimens collected on successive days were in every case negative on direct examination for tubercle bacilli, but monilias were constantly present. The type of monilia was identified following culture on Sabouraud's medium as *monilia albicans*. It was found to be pathogenic to rabbits according to the method of Castellani (*vide infra*).

Sputum obtained by bronchoscopic aspiration did not contain *monilia albicans* either on direct examination or on culture on Sabouraud's medium.

Six cultures on Loewenstein's medium for tubercle bacilli were negative.

Six guinea-pigs were inoculated with preparations of the sputum at different times. On post-mortem examination, five had no evidence of tuberculous infection, but the sixth had a nodule in the spleen from which tubercle bacilli were isolated. In view of this anomalous finding, it was decided to inoculate six more guinea-pigs, but the patient died before this could be done. It is probable that some mistake in identity occurred with the sixth guinea-pig. In the bacteriologist's opinion, based on the previous as well as the present investigations, the sputum could be held not to contain tubercle bacilli.

It was therefore decided that the provisional diagnosis of pulmonary tuberculosis was incorrect. In view of the sputum findings, pulmonary moniliasis was suspected and the following investigations were performed:—

1. *Blood Culture.* Negative for monilia.
2. *Production of Fixation Abscess.* No abscess occurred on injection of digitalin subcutaneously.
3. *Serum Agglutination.* This was negative against both a standard strain of *monilia albicans* and the *monilia albicans* isolated from the patient.
4. *Skin Test.* Intradermal injection of a preparation made from a stock culture of *monilia albicans* gave no reaction.
5. *Therapeutic Test.* Potassium iodide by mouth was not tolerated by the patient and hence it proved impossible to give this an extensive trial.

**CLINICAL COURSE.**—This was steadily downhill. A rising blood urea with polyuria and impaired renal function tests suggested that



uræmia was resulting from amyloid contracted kidneys. Death occurred on 27th April 1947.

**AUTOPSY REPORT.**—A. *Macroscopic.* Both pleural cavities were almost obliterated by dense adhesions.

The bronchi contained muco-purulent material from which *monilia albicans* was not isolated either on direct examination or on culture.

The upper and middle lobes of the right lung were almost replaced by several large cavities which contained a small amount of fairly thick purulent fluid from which *monilia albicans* could not be isolated. The walls of the cavities were formed by fibrous tissue. No tubercles or areas of caseation could be found either in the lungs or in the swollen hilar lymph nodes. Similar but less marked changes were found in the left upper lobe. The remainder of the lungs showed congestion, chronic bronchitis and emphysema.

The liver and spleen were typical of amyloid disease. The kidneys were amyloid contracted in type.

The other organs showed no significant changes.

B. *Microscopic.* Tissue from all parts of the right lung was examined but failed to reveal any signs of tuberculosis. The various cavities all showed a similar structure :—

1. A well-defined inner zone of vascular granulation tissue.
2. An outer zone of dense fibrous tissue which was as a rule relatively narrow.

In none of the cavities could any histological evidence of tuberculosis be found. Gram-Weigert sections of the various cavities and bronchial lymph nodes failed to reveal *monilia albicans*.

The structure of the cavities very strongly suggested that they were of bronchiectatic origin.

The presence of amyloidosis was confirmed in the liver, spleen and kidney.

The final diagnosis was therefore bronchiectasis with amyloid disease.

**DISCUSSION.**—The central theme of all discussions on pulmonary moniliasis is the significance of the finding of *monilia albicans* in the sputum. The Flinns (1935) in a review of the literature point out that *monilia* may be found very frequently in the normal mouth and throat, so that the mere presence of *monilia* in sputum is not sufficient evidence to establish a diagnosis of pulmonary moniliasis. Keiper (1938) found that 3 per cent. of normal people harbour *monilia* in the throat. Doub (1940), discussing the radiology of the condition, states that "it should be emphasized that the presence of fungi in the sputum does not in itself justify the diagnosis of primary fungus infection, but it should indicate further studies to determine what role they play in the patient's problem."

It is fortunate that this point has been consistently emphasised

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by so many writers, since the finding of *monilia albicans* in the sputum appears to be a common phenomenon. Marett (1933) working in Jersey found that out of 568 routine sputum examinations, 294 (51 per cent.) contained *monilia albicans*. This extraordinarily high figure may have been determined by local conditions, a more representative example being 7 out of 141 (5 per cent.) quoted by Woolley (1938) in an investigation carried out in America.

It is thus universally agreed that the finding of *monilia* in the sputum must be followed up by certain investigations to attempt to determine its significance.

Castellani (1912) who first described cases of pulmonary moniliasis in tea-tasters in Ceylon, suggested that monilias in the sputum fell into three categories :—

1. Non-pathogenic and non-virulent.
2. Secondary invaders.
3. Virulent and basis of disease.

Monilias were placed in the third category only when they produced lesions in the lungs of inoculated animals. Similarly, the Flinns (1935) insist that a diagnosis of pulmonary moniliasis is justified only by the constant finding in the sputum of monilias which produce in rabbits on intra-pulmonary inoculation pulmonary nodules from which monilias can subsequently be recovered.

The postulates of Castellani and the Flinns appear to have been accepted as a basis in diagnosis by most writers, but it would seem unwise to accept without question that a *monilia* is the cause of pathological changes in the human lung because it is capable of producing such changes in the lung of a rabbit. In the case report given above, a *monilia* was recovered consistently from the sputum and proved to be virulent to rabbits in the manner postulated. The final diagnosis, however, was bronchiectasis and not pulmonary moniliasis.

It is insufficiently stressed in the literature that precautions should be taken to prevent contamination of the sputum from the mouth and throat. The Flinns (1935) suggest that the mouth and throat should be cleansed by gargling, but this would seem an ineffective method of dealing with the problem. A significant finding in the present case is that sputum removed directly from the lungs by bronchoscopy and at autopsy did not contain *monilia*. It is suggested that bronchoscopic aspiration is an essential part of the procedure in a case of suspected pulmonary moniliasis.

It is clear that great difficulties arise in the interpretation of the finding of *monilia albicans* in the sputum, and that no certain diagnosis comparable to the diagnosis of pulmonary tuberculosis when tubercle bacilli are found in the sputum, is possible. It is therefore appropriate to discuss other features by which *monilia* infection of the lungs can be suspected or diagnosed.

CLINICAL FEATURES.—Ikeda (1936) states that cases fall into three main groups :—

1. *Mild Form*. Characterised by cough and scanty spit.
2. *Moderate Form*. Characterised by cough, tenacious mucopurulent spit and low-grade fever.
3. *Severe Form*. Characterised by dyspnoea, night sweats, cough, loss of weight and sputum which is sticky and glairy; in the main this form pursues a chronic course which may be interrupted by acute exacerbations resembling acute lobar pneumonia.

It is clear that none of these forms presents any feature which is characteristic. The mild form resembles ordinary chronic bronchitis, and the moderate and severe forms resemble bronchiectasis and pulmonary tuberculosis. Physical signs in the chest, about which most writers are vague, are similarly unhelpful, and vary from those of mild chronic bronchitis to those of advanced cavitation and fibrosis such as would be found in pulmonary tuberculosis or bronchiectasis.

Since monilias are frequently found as secondary invaders in the sputum of patients suffering from those other chronic diseases, it is not surprising that many cases described in the literature as pulmonary moniliasis may well have had a more important underlying pathology.

In contrast to those non-specific clinical features, Gow Brown (1946), who isolated monilia albicans from 467 sputa in the course of one year of routine bacteriological work, claims that such sputa have a characteristic appearance which is likened to "watered milk with a white flocculent deposit." On microscopic examination the flocculent deposit is found to consist of epithelial cells and macrophages without polymorphs and lymphocytes, provided that secondary pyogenic infection is absent. It is curious that this apparently obvious feature has not been recorded before, unless the explanation is geographical, such sputum occurring only in Gow Brown's territory in Lanarkshire. It remains to be proved that monilias in such sputum are the cause of pathological changes in the lungs. In the advanced case with cavities and secondary infection akin to the present writer's suspected case, the sputum could not of course retain such an appearance.

In most lung conditions, radiology has proved of inestimable value in diagnosis, but this does not apply in moniliasis in which there is apparently no pathognomonic change. Ikeda (1936) dismisses the subject briefly by stating that the X-ray appearances vary from those of chronic bronchitis to those of fibrosis, emphysema and bronchiectatic cavities. Doub (1940), after remarking that the appearances closely simulate those of pulmonary tuberculosis, describes marked enlargement of the hilar areas with extensive infiltration extending throughout the lungs but less marked at the apices; he adds that small cavities may occur but are uncommon. Carter (1936), on the other hand, claims that apical lesions are common along with hilar thickening, interstitial fibrosis and bronchiectatic cavitation. It is clear that the

radiological appearances may simulate any chronic lung pathology. Moreover, it is doubtful, in view of the too ready acceptance of a diagnosis of moniliasis when monilias are present in the sputum, if some radiological descriptions in the literature are really those of moniliasis.

Other aids to diagnosis which were negative or unhelpful in the case described above are :—

1. *Blood Culture*. Wessler and Browne (1945) report an interesting case of a chronic asthmatic who developed a severe bronchitis without X-ray changes. Monilia were isolated from the sputum, throat and blood. It is suggested that the asthma was due to allergy to monilia and that the bronchitis was due to a monilia infection of the bronchi.

Provided that precautions are taken to ensure that no contamination of the blood culture occurs by ubiquitous monilia, it would seem that a positive result may be interpreted as invasion of the body by a virulent monilia capable of causing pathological changes.

Joekes and Simpson (1923) also comment on the confirmatory value of a positive blood culture.

The case reported by Wessler and Browne also had monilia in the stool and urine, but as they rightly point out, the risk of contamination is so great that no reliance can be placed on positive findings.

2. *Production of Fixation Abscess*. Joekes and Simpson (1923) recommend subcutaneous injection of digitalin to produce a fixation abscess from which monilia may be recovered. It would seem that this method is likely to give positive results only when the blood culture is positive, but may in some cases be a more sensitive indication of generalised infection.

3. *Serum Agglutination*. Ikeda (1936) states that the serum of a patient suffering from moniliasis may agglutinate a stock monilia albicans.

4. *Skin Test*. This is performed in a manner similar to the Mantoux test with an extract from a stock culture of monilia albicans. When the test is positive, difficulties in interpretation akin to a positive Mantoux arise, and hence it is of little or no value.

5. *Therapeutic Test*. Wylie and De Blase (1944) describing a case said to be pulmonary moniliasis comment on the remarkable improvement following the oral administration of potassium iodide. While this particular case is open to criticism regarding diagnosis, it seems reasonable to suppose that a chronic lung condition which responds dramatically to potassium iodide is not likely to be any of the common lung diseases and hence it might well be due to fungus infection.

6. *Autopsy Findings*. Boggs and Pincoffs (1915) published the first autopsy report of pulmonary moniliasis. Unfortunately the findings in their case were not straightforward since the patient also had a carcinoma of left breast. She developed a suppuration in the left axilla which extended into the left lung and pleural cavity. Monilias

pathogenic to rabbits were found in the sputum. At autopsy there were two large abscesses communicating between the supraclavicular and infraclavicular regions and both communicated through the chest wall with the lung. The upper lobe was densely consolidated and microscopy revealed an exudate of fibrin, mononuclear and polynuclear cells. *Monilia albicans* was demonstrated in the lesions.

It seems clear that their case was not one of primary moniliasis of the lung but rather a secondary involvement of the lung by direct extension from a nearby lesion. Although there is no specific mention of it, one wonders if secondary carcinoma in the axillary glands did not predispose in some way to monilia infection.

Ikeda (1936) states that no lesions which may be construed as specific or peculiar to pulmonary moniliasis have been described. The commonest findings are those occurring in any chronic lung disease, *i.e.* emphysema, thick adherent pleura and diffuse fibrosis, plus areas of pneumonic consolidation with small cavities and abscesses and occasionally larger bronchiectatic cavities. Microscopically there is severe bronchitis, peribronchial fibrosis and bronchiectasis. Areas of consolidation with small cavities consist mainly of chronic inflammatory cells unless there is secondary infection when polymorphs appear. Monilias are found in the walls of abscesses, in the bronchial walls and in the regional lymph nodes.

Mendelson (1921) examined the lungs of a number of persons who were said to have pulmonary moniliasis and who died of other causes. He found small mycotic tumour nodules which had not broken down. These nodules are comparable to those produced in rabbits by intra-pulmonary inoculation of monilia.

It is clear that in the ordinary chronic case the autopsy findings are most indefinite apart from the demonstration of monilia in the lesions. Even in that important point, difficulties arise, since Ikeda (1936) found that in 12 out of 40 control cases dying of advanced pulmonary tuberculosis or cancer monilia *albicans* was also found in the lesions. Ikeda and Boggs and Pincoffs refer to the difficulty in demonstrating monilia in the lesions by ordinary staining methods such as hæmatoxylin eosin, and recommend the use of Gram-Weigert stain. In the present writer's case, monilia could not be demonstrated even with Gram-Weigert stain.

**SUMMARY.**—A case report and a review of the literature have been presented to emphasise the formidable difficulties which arise in the diagnosis of pulmonary moniliasis.

Most writers on the subject are content to stress the need for a skilled bacteriologist to assist in diagnosis. It would seem, however, that the bacteriologist's part is of minor importance, since there is no great difficulty in isolating monilia from sputum, and animal virulence tests have to be accepted with great reserve. The finding of monilia by the bacteriologist is merely the first step in the investigation.

The next step is to determine, by examination of sputum aspirated

through a bronchoscope, whether the monilias are coming from the lungs or from the pharynx or mouth.

Should the bronchoscopic findings be positive, the diagnosis is not necessarily proved, since the monilia may be a secondary infection in an underlying tuberculous, neoplastic or bronchiectatic lesion. Appropriate investigations, which may be inconclusive until autopsy is performed, are necessary to exclude these other chronic lung conditions. At autopsy, it is important to remember that monilias require special staining methods for their demonstration.

In conclusion, it may be said that it is doubtful if primary pulmonary moniliasis really exists. It seems reasonable to postulate, however, that when secondary invasion of other pulmonary lesions is proved by bronchoscopic methods, the monilias may contribute to their chronicity.

I am indebted to Dr W. Forbes for a summary of the autopsy findings and to Dr J. C. J. Ives for the extensive bacteriological investigations.

I wish to thank Professor Charles Cameron and Dr J. D. S. Cameron for their advice and criticism and Dr W. D. D. Small for permission to publish the case.

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# THE BLOOD AND BONE MARROW IN THE SPRUE SYNDROME

## A STUDY OF 63 CASES

By ELIZABETH M. INNES, M.B., M.R.C.P.E.

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THE sprue syndrome consists of a symptom complex rather than a disease entity. The chief characteristics of the condition are fatty diarrhœa, wasting, anæmia and various vitamin deficiencies. It occurs in tropical sprue, non-tropical sprue and cœliac disease, in none of which is there any demonstrable lesion of the alimentary tract. The ætiology of these conditions is still obscure, but there appears to be general agreement that they are associated with a state of "jejuno-ileal insufficiency" (Bennett and Hardwick, 1940). There is a wide divergence of opinion as to whether tropical and non-tropical sprue are merely geographical variants of the same disease, and also as to whether non-tropical sprue is a separate condition from cœliac disease or simply a continuation of the latter condition into adult life. In discussing the blood picture in the sprue syndrome, however, it is simpler to assume that the three conditions are, in fact, separate though closely allied disorders.

Anæmia has for long been recognised as a cardinal manifestation of tropical sprue, but it is only comparatively recently that detailed studies of both peripheral blood and bone marrow have been made in patients suffering from this condition. It is evident from the literature that the anæmia most often found is of the macrocytic type, and bears a strong resemblance to pernicious anæmia (Manson-Bahr, 1941). In a series of 198 cases of tropical sprue Manson-Bahr and Willoughby (1930) found a colour index of unity or over in every instance. Rice (1943), in a review of 365 cases reported in the literature, found that a macrocytic anæmia was present in over 90 per cent. of cases, in most instances morphologically identical with pernicious anæmia. In 1935, Castle *et al.* reported in detail on a series of 92 sprue patients in Puerto Rico, selected because of the severity of their symptoms. They concluded that the typical blood picture in this series was a macrocytic anæmia, but with less poikilocytosis and less tendency to associated leucopenia than is usual in pernicious anæmia. A megaloblastic marrow reaction was found in all 22 cases on whom sternal punctures were performed. It is suggested by Castle and his colleagues that three factors are involved in the ætiology of this megaloblastic anæmia :—

- (a) Deficient intake of the extrinsic factor.
- (b) Defective production of the intrinsic factor.
- (c) Defective absorption of the hæmopoietic principle.

They claim that all three defects may be overcome by the administration of large doses of parenteral liver, although they point out that the resulting improvement in the blood level may be much slower than occurs in pernicious anæmia. More recently Keele (1946), in a series of 80 cases of early sprue studied in India, has reported macrocytic anæmia in 26 per cent., macrocytosis in the absence of anæmia in 30 per cent., normal blood counts in 35 per cent., and a hypochromic anæmia in 9 per cent.

In contrast to the wealth of information regarding the blood picture in tropical sprue, reports on the blood findings in non-tropical sprue are mostly scanty, inadequate and conflicting. Hanes (1942) states that anæmia when present is practically always of the macrocytic type and cannot be distinguished from pernicious anæmia either in the peripheral blood or in the bone marrow. Barker (1943), on the other hand, claims that, although macrocytic anæmia may occur, normocytic or microcytic anæmia is much more common. Thaysen (1935), reviewing 45 cases, reports a "hyperchromic" anæmia with a colour index over unity in 30 of them, while in a series of 10 cases Moore *et al.* (1936) found that 5 had a hypochromic anæmia and 2 had a "hyperchromic" anæmia.

Most authors are agreed that the anæmia associated with coeliac disease is generally of the hypochromic microcytic variety. Thaysen (1931) reported this type of anæmia in 21 out of 29 cases of coeliac disease. A further 39 cases were described by Fanconi (1928). He found that 29 of them had a colour index of below 0.9, but that 3 had blood findings comparable to severe pernicious anæmia. Dalton *et al.* (1946) have described 2 cases of coeliac disease in which a megaloblastic marrow was found. This, however, is a rare occurrence, and the same authors in a personal communication report that sternal punctures carried out subsequently on a further 15 cases revealed a normoblastic marrow reaction in every case.

From this short review of the literature it appears that the frequent occurrence of megaloblastic anæmia among cases of sprue in the tropics is established. On the other hand, the blood picture in the sprue syndrome as met with in this country is much less well defined, and it was in an attempt to throw some light on this problem that the following investigation was undertaken. Since the completion of the investigation, an account of the blood picture in 45 cases of idiopathic steatorrhœa has been published by Cooke *et al.* (1948).

#### SCOPE OF THE INVESTIGATION

During the past year we have studied the hæmatological findings in a series of 63 cases of the sprue syndrome, some in hospital and some as out-patients. The hospital patients were referred to us because of symptoms of diarrhœa, anæmia, etc. The out-patients were asked to report for examination because they had at some earlier date been

diagnosed as suffering from the sprue syndrome. Forty-three of these cases were adults, of whom 16 had tropical sprue and 27 had non-tropical sprue. The 19 children in the series all suffered from coeliac disease.

In each adult patient a full blood count was carried out on a venous sample oxalated by Wintrobe's mixture. In a few cases examination of the blood had to be delayed longer than is desirable for an accurate estimation of the white cell count, and in these cases the figures for the white count are therefore omitted. Capillary blood counts were carried out on the children, owing to the difficulty of obtaining venous samples.

Each patient was examined in an attempt to correlate clinical features with hæmatological findings. In addition, certain of the cases in the series have been under our care in hospital either before or subsequent to the date of the investigation outlined above. This has afforded us an opportunity of studying the bone marrow cytology, and also of observing the changes which occurred in the marrow and peripheral blood in response to treatment.

The hæmoglobinometer employed in these investigations was of the Haldane pattern, standardised by the N.P.L. (100 per cent. = 13.8 gms. Hb. per 100 ml.).\*

### THE PERIPHERAL BLOOD

Group I consisted of 17 patients whose ages ranged from twenty-two to seventy. Of these, 9 were men and 8 were women. All had at one time been in the tropics, and a diagnosis of tropical sprue had been made in hospital either in Great Britain or abroad. Treatment by dietetic means and with liver therapy had been carried out in every case at some stage of the illness. Only 7 of these patients were having diarrhoea at the time of examination. Of the remaining 10, 2 were completely symptom-free (cases 13 and 15). The rest complained of lassitude, flatulence, intermittent acute glossitis, etc.

The first striking feature about the peripheral blood picture in this group was the absence of any very marked degree of anæmia. The lowest hæmoglobin (Hb.) recorded was 64 per cent. (Haldane) and the mean Hb. was 90.5 per cent. The incidence of macrocytosis was, however, very high. A colour index (C.I.) of above 1.10 was found in 10 cases, and the mean cell volume (M.C.V.) was greater than 92 c. $\mu$  in 13 out of 16 cases. In no instance did the mean corpuscular hæmoglobin concentration (M.C.H.C.) reveal any marked degree of iron deficiency, and in only one case (case 10) was the white cell count significantly reduced. The erythrocytes in the stained blood film exhibited a varying degree of macrocytosis with little aniso- or

\* The recent work of King *et al.* (1947) suggests that 100 per cent. on the Haldane scale represents 14.4 or 14.8 gms. Hb. per 100 ml. according to the method of analysis employed.

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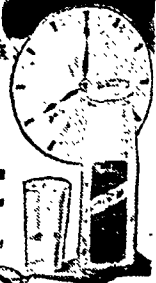
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poikilocytosis. No nucleated red cells were seen. The appearances were, in fact, very similar to those seen in a case of pernicious anæmia at a comparable hæmoglobin level, except that macrocytosis was more marked among the sprue cases. Differential counts revealed no deviation from normal in the white cells.

One further point of interest deserves comment. Cases 1-10 were all at the time of examination receiving regular injections of liver extract at intervals of not longer than a week. This dosage would be more than sufficient to maintain a case of pernicious anæmia at a completely normal erythrocyte level, yet in not one of these cases had such a level been reached, the blood picture remaining persistently macrocytic in 8 of them.

TABLE I  
*Group I—Tropical Sprue*

Case No.	Sex.	Age.	Hb. per cent.	R.B.C. in Mills.	C.I.	M.C.V. in c.µ.	M.C.H.C. per cent.	W.B.C. in Thousands.	Liver Therapy.	Duration of Condition in Years.	Presence of Diarrhœa.
1	M	52	106	4.77	1.11	94.1	32.5	6.8	+	29	+
2	F	42	80	3.75	1.07	93.0	31.5	10.4	+	22	—
3	M	35	102	3.73	1.37	112.6	33.5	5.2	+	3	+
4	M	69	94	3.69	1.27	103.0	34.0	4.2	+	30	—
5	M	64	100	3.98	1.26	110.6	31.3	6.8	+	7	—
6	M	59	78	3.30	1.18	103.0	31.6	5.0	+	18	+
7	F	70	78	3.22	1.21	107.1	31.3	5.0	+	16	+
8	F	59	80	3.48	1.14	...	...	5.0	+	30	+
9	F	31	86	4.57	0.93	91.9	28.5	7.8	+	2	—
10	M	26	64	2.70	1.18	100.0	32.7	2.2	+	3	+
11	M	40	116	5.08	1.14	92.5	34.0	...	—	2	—
12	F	61	90	4.58	0.98	90.6	29.9	5.8	—	27	+
13	M	22	102	5.22	1.07	99.6	29.7	6.6	—	2½	—
14	M	53	98	4.37	1.12	100.7	30.7	10.0	—	16	—
15	F	50	102	4.85	1.05	93.8	31.0	8.2	—	8	—
16	F	50	70	3.57	0.98	84.0	32.2	4.8	—	17	—
17	F	50	92	4.46	1.04	97.5	29.2	5.2	—	1	—

The factors which, it was felt, might possibly affect the degree or type of anæmia present were (a) the duration of the condition, and (b) whether or not the patient was suffering from diarrhœa at the time when the blood was examined. A study of Table I, however, reveals that no such correlation can be shown to exist.

In Group II we had 27 patients whose ages ranged from 34 to 68. The sex incidence showed a striking preponderance of males, there being 21 men and 6 women. None of these patients had ever been in the tropics, and all had been diagnosed and treated as cases of non-tropical sprue in hospitals in this country. It is of interest to note that in only one case (No. 34) could any history suggestive of cœliac disease in childhood be elicited. On the other hand, several of these patients showed a dwarfing of the skeleton which might well have been due to malabsorption during the growth period. Diarrhœa was present at the time of examination in 12 cases. Of the other 17, 8

claimed to be symptom free (cases 20, 27, 30, 31, 36, 38, 42 and 43). The rest complained of lassitude, flatulence and abdominal distension, painful tongue, etc.

On examining the blood of this group of patients we found that the incidence of anæmia was higher and the degree more severe than among the tropical group. The most anæmic patient had an Hb. of 44 per cent., and the mean Hb. figure was 77.8 per cent. Macrocytosis was again a striking feature, the M.C.V. being above 92 c. $\mu$  in 18 cases. A C.I. of over 1.10 was, however, found in only 11 instances,

TABLE II  
*Group II—Non-Tropical Sprue*

Case No.	Sex.	Age.	Hb. per cent.	R.B.C. in Mills.	C.I.	M.C.V. in c. $\mu$ .	M.C.H.C. per cent.	W.B.C. in Thousands.	Liver Therapy.	Duration of Condition in Years.	Present of Diarrhoea
18	F	68	70	3.22	1.00	96.3	20.0	4.6	+	25	+
19	M	54	80	4.53	0.88	80.0	30.7	6.6	+	8	+
20	M	49	86	3.74	1.15	95.0	33.4	5.2	+	12	—
21	M	53	72	2.70	1.20	128.3	30.0	5.6	+	2½	—
22	M	52	76	3.51	1.08	105.4	28.0	6.2	+	4	+
23	M	50	84	3.10	1.30	109.9	30.2	6.6	+	4½	+
24	M	46	90	3.64	1.20	105.4	30.0	2.4	+	12½	+
25	M	35	90	3.23	1.30	111.5	34.5	...	+	2½	—
26	F	61	68	3.48	0.97	92.0	29.3	10.8	+	7	+
27	M	55	68	3.11	1.09	108.0	28.0	7.2	+	6	—
28	F	37	78	3.35	1.17	104.5	30.7	8.0	+	1	—
29	M	47	112	5.38	1.04	87.3	32.9	4.4	+	1½	+
30	M	38	98	4.75	1.03	93.7	30.3	6.2	+	2½	—
31	F	47	88	4.55	0.97	90.2	29.7	6.0	—	27	—
32	M	55	84	3.62	1.16	104.9	30.5	...	—	5	+
33	M	41	70	3.48	1.00	93.4	29.1	7.2	—	2	—
34	F	48	82	4.18	0.98	93.3	29.0	...	—	40+	+
35	M	38	50	1.85	1.35	124.3	30.0	5.0	—	6	+
36	M	68	94	4.71	0.99	87.1	31.6	12.8	—	30	—
37	F	37	44	1.49	1.48	134.2	30.3	8.4	—	2½	+
38	M	41	96	4.18	1.15	100.5	31.5	...	—	3	—
39	M	43	80	3.80	1.05	102.6	28.3	6.8	—	3	—
40	M	59	72	4.31	0.83	83.5	27.5	...	—	3	—
41	M	34	56	4.59	0.61	70.8	23.7	8.4	—	17	—
42	M	46	70	4.41	0.80	83.9	26.1	5.8	—	6	—
43	M	38	86	3.87	1.11	102.1	30.0	7.0	—	4	—
44	M	59	58	4.11	0.70	80.5	24.2	6.8	—	3	+

due to the presence of a superadded iron deficiency (as evidenced by the M.C.H.C.) in certain of the macrocytic cases. Moreover, there were in this group 4 cases (Nos. 40, 41, 42 and 44) in which the anæmia present was of the hypochromic normocytic type. There was no evidence of blood loss in these patients with the exception of case 44, in whom bleeding hæmorrhoids was a complicating factor. In only one case (case 24) was leucopenia a significant finding.

Examination of the blood film revealed some interesting features which were not observed in the tropical group. The typical picture showed fully stained macrocytic red cells, with hypochromic microcytic cells present in varying proportions. In many cases there were, in

addition, considerable numbers of target cells present, the whole giving rise to a highly characteristic appearance. A rather curious feature in 4 cases (21, 37, 39 and 40) was the finding of many normoblasts and Howell-Jolly bodies. Differential white cell counts revealed no abnormality, either quantitative or qualitative.

As in the previous group, attention may be drawn to the blood findings in those patients (cases 18-30) who were receiving regular liver therapy at the time of examination. In only one of these had the red cell count reached 5 million per c.mm., and in 10 out of 13 cases it remained below 4 million. That the red cells were in most cases macrocytic is shown by the fact that of the 13 treated cases, 10

TABLE III  
*Group III—Celiac Disease*

Case No.	Sex.	Age.		Hb. per cent.	R.B.C. in Mills.	C.I.	W.B.C. in Thousands.	Iron Therapy.	Duration of Condition.		Diarrhoea.
		Yrs.	Mths.						Yrs.	Mths.	
45	M	1	10	56	5.23	0.54	12.0	+	...	10	+
46	F	2	8	80	4.34	0.92	9.8	+	1	9	+
47	F	5	3	76	4.04	0.93	12.6	+	4	3	—
48	M	4	...	66	4.24	0.78	10.8	—	2	2	—
49	M	3	...	58	4.64	0.63	11.8	—	1	3	—
50	F	4	...	64	5.61	0.57	10.2	—	2	10	—
51	F	3	4	52	4.53	0.58	10.8	—	2	3	—
52	F	7	4	58	4.68	0.62	7.2	—	6	...	—
53	F	4	9	78	4.70	0.83	6.8	—	4	...	—
54	F	5	2	90	5.04	0.90	9.6	—	4	...	—
55	F	8	6	96	4.89	0.98	8.2	—	7	5	+
56	M	4	11	72	4.31	0.84	13.6	—	4	6	—
57	M	7	6	90	5.40	0.83	6.8	—	7	...	—
58	F	12	6	50	5.20	0.48	12.8	—	11	3	—
59	F	11	1	80	4.42	0.90	7.8	—	10	2	—
60	F	3	3	68	4.03	0.84	6.8	—	1	3	+
61	F	2	9	76	5.02	0.76	7.6	—	1	...	—
62	F	6	4	58	4.32	0.67	9.4	—	5	2	—
63	F	9	6	56	5.23	0.54	7.8	—	8	1	—

had an M.C.V. of over 92 c. $\mu$ . Details as to duration of the condition and presence or absence of diarrhoea are included in Table II, but here again they appear to have no bearing on either the degree or the type of anæmia present.

The third group of patients consisted of 19 children, whose ages ranged from 1<sup>10</sup>/<sub>12</sub> to 12<sup>6</sup>/<sub>12</sub> years. Of these, 14 were girls and 5 were boys—a striking reversal of the sex ratio found in the adult group of non-tropical sprue. It might be suggested in passing that this is a definite point against the theory that the latter condition represents celiac disease continued into adult life. The children had all been satisfactorily diagnosed as cases of celiac disease in infancy, and had received hospital treatment for varying periods. Cases 45, 46, 60 and 61 were still in hospital when examined. The rest were seen as out-patients, and were for the most part symptom-free except for a



persistent tendency to abdominal distension and the occasional passage of a bulky stool. In view of the general absence of clinical features, we were surprised to find a widespread incidence and in some cases a severe degree of anæmia among these children. The most anæmic patient had an Hb. of 50 per cent., and the mean figure for the series was 69.7 per cent. There was, however, little quantitative deficiency of erythrocytes, the red cell count being over 4 million per c.mm. in every case. The anæmia present was therefore of the hypochromic microcytic variety.

Total and differential white counts revealed no abnormality. The red cells were typically hypochromic and microcytic, though in a few cases there was also a small proportion of fully stained macrocytes. A highly characteristic feature was the presence of target cells. These appeared in significant numbers in every anæmic case, and were particularly prominent in cases 45, 49, 50, 58, 59 and 63 (constituting up to 25 per cent. of the erythrocytes in some fields).

Since only 3 children in this group were having iron therapy at the time of examination it was hoped that much benefit would result from the regular administration of this hæmatinic. Iron therapy has, however, generally proved unsuccessful; several of the more anæmic cases have been given iron in the form of ferrous sulphate by mouth over long periods, and the anæmia has remained completely refractory.

### THE BONE MARROW

We have carried out sternal marrow biopsies on 18 of the adult cases in our series, in some instances on more than one occasion. The results obtained are set out in Table IV. In many cases the date of marrow examination did not correspond to the date of blood examination detailed above. Where this is so, time relationships and relevant blood counts are given. No attempt will be made in the following description to distinguish between tropical and non-tropical cases, as the marrow findings were similar in the two conditions.

The term "megaloblastic" has been applied to a marrow only when it was found to contain large numbers of early and intermediate megaloblasts. The latter (Ehrlich megaloblasts) are highly characteristic, being partially hæmoglobinised cells whose nucleus shows a very open chromatin network. This marrow picture was found in 9 cases. It will be noted that all of these had a considerable degree of anæmia which was frankly macrocytic. (Case 15, with a C.I. of 1.00, had an M.C.V. of 100 c. $\mu$ .) With the exception of cases 10 and 44, no patient with a frankly megaloblastic marrow had received any liver therapy prior to sternal puncture. Cases 10 and 44 were examples of refractory megaloblastic anæmia (Davidson *et al.*, 1943) which failed to respond to parenteral liver therapy but which subsequently responded to folic acid.

Of the remaining 9 cases, 5 had a normoblastic marrow, whilst 4

had a marrow picture which we call "intermediate" for descriptive purposes. In addition, case 4, which initially showed a megaloblastic reaction, presented the "intermediate" marrow picture when examined after five and a half years of continuous liver therapy.

This "intermediate" marrow picture is characterised by the presence of considerable numbers of "intermediate erythroblasts." The latter cell, though smaller than a megaloblast, is still large, and its nuclear chromatin is slightly condensed as compared with the megaloblast. The amount of nuclear condensation is, however, not so great as would be found in a normoblast at the corresponding stage of development (as judged by the degree of hæmoglobinisation present).

TABLE IV  
*Marrow Findings in Adults*

Case No.	Time of Examination.*	Hb. per cent.	R.B.C. in Mills.	C.I.	Marrow Type.	Liver Therapy.
4	(a) 6 yrs. previously	65	2.55	1.25	Megaloblastic	—
	(b) 6 mths. "	80	3.30	1.21	"Intermediate"	+
6	Coincidental	78	3.30	1.18	"Intermediate"	+
7	Coincidental	78	3.22	1.21	Hypoplastic normoblastic	+
10	Coincidental	64	2.70	1.18	Megaloblastic	+
15	4 yrs. previously	50	2.48	1.00	Megaloblastic	—
16	Coincidental	70	3.57	0.98	Normoblastic	—
20	2 yrs. previously	54	2.13	1.27	Megaloblastic	—
23	(a) 1 yr. previously	70	2.90	1.21	"Intermediate"	+
	(b) 10 mths. "	64	2.61	1.20	"Intermediate"	+
	(c) Coincidental	84	3.19	1.30	"Intermediate"	+
25	Coincidental	90	3.23	1.39	Normoblastic	+
26	Coincidental	68	3.48	0.97	Hypoplastic normoblastic	+
29	9 mths. previously	60	2.40	1.25	Megaloblastic	—
35	Coincidental	50	1.85	1.35	Megaloblastic	—
37	Coincidental	44	1.49	1.48	Megaloblastic	—
38	1 yr. previously	62	2.42	1.28	Megaloblastic	—
39	2 yrs. "	64	2.92	1.10	"Intermediate"	+
40	18 mths. "	72	3.00	1.20	"Intermediate"	+
41	2 yrs. "	60	2.96	1.00	Normoblastic	—
44	1 yr. "	28	0.95	1.47	Megaloblastic	+

\* In relation to counts in Tables I and II.

Such an "intermediate" marrow picture is comparable to that seen in a case of pernicious anæmia in relapse following the injection of a sub-optimal dose of liver extract. It is therefore of particular interest to note, that in our series, this type of marrow was characteristically found in cases which were receiving regular liver injections, but which nevertheless manifested a persistently macrocytic blood picture associated with a moderate degree of anæmia.

A frankly normoblastic reaction was present in the marrow of cases 16, 25 and 41. The blood picture in case 25 was characterised by macrocytosis in the absence of anæmia. In the other 2 cases there was a moderate degree of normocytic anæmia. Finally, in 2 cases (Nos. 7 and 26) the marrow was hypoplastic, such erythroblasts as were present being of the normoblast series. Both these patients were

3. The marrow picture is described in 18 of the adult cases. It was megaloblastic in 9 cases (2 of which had previously had liver therapy), normoblastic in 5 cases, and "intermediate" in 4 cases. The use of the latter term is explained.

The marrow was found to be normoblastic in both of the cases of coeliac disease in which it was examined.

4. The significance of these findings is discussed.

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## INTRA-UTERINE PENICILLIN

By M. M. KRISEMAN, M.B., B.CH.(Wits.), F.R.C.S.Ed., M.R.C.O.G.

THE ready absorption of penicillin from serous surfaces has led to the wide adoption of its local administration in many instances. It has been shown (Florey and Heatley) that effective bacteriostatic levels in the blood have been obtained by injecting penicillin into empyema cavities, abscesses, infected joints, and into the spinal theca. The advantage of treating an infected cavity locally and at the same time being able to secure a systemic effect will be at once apparent.

An investigation into the local treatment of wounds with penicillin (Florey *et al.*) demonstrated that a high concentration was achieved locally, and at the same time a constant inhibiting level in the blood maintained by regular instillations. They concluded that penicillin was readily absorbed from wounds, and must traverse their walls, inhibiting meanwhile organisms lying in its path to gain access to the blood and urine. The fact that this state of affairs is closely analogous to that in the uterine cavity in certain post-abortal and puerperal infections, prompted the desire to investigate the absorbability of penicillin from the uterine cavity and to assess its possible clinical application.

It has been long appreciated that the uterine cavity provides an efficient surface for absorbing drugs. The danger of using mercurial salts in an intra-uterine douche has been pointed out (Johnstone). Sulphonamides are likewise readily absorbed, and, it has been shown (Sadovsky *et al.*), provide an effective local and blood stream concentration.

It is proposed to show that penicillin applied locally is similarly absorbed, and that an effective bacteriostatic level can be obtained in the blood stream. The intra-uterine musculature after abrasion of its surface following abortion, removal of placental tissue or curettage, appears to offer a ready surface for this purpose. The advantages in certain respects of local administration over the systemic use of penicillin will be outlined and suggestions offered as to its clinical application. Other investigators have demonstrated the ready adsorption of penicillin from the genital tract. Rune and Frisk instilled penicillin into the Fallopian tubes following operations for sterility. Effective bacteriostatic levels were obtained in the blood. Similarly by the use of vaginal suppositories, Rock, Barker and Bacon secured therapeutic blood levels.

In this series of cases comprising 7 cases of incomplete abortion,

\* Read at a meeting of the Edinburgh Obstetrical Society on Wednesday, 14th January 1948.

1 case of septic abortion, 2 cases of local uterine puerperal infection and 1 case of functional uterine bleeding, the effect of intra-uterine instillation of penicillin was observed.

### TECHNIQUE OF ADMINISTRATION

Two methods of instillation were adopted: (a) the continuous and (b) the intermittent.

The patient was prepared routinely for operation, and swabs taken for culture from the posterior fornix and cervical canal before any vaginal toilet had been carried out. Following the appropriate operative procedure for each individual case, a rubber catheter, a No. 8 (English) chosen as a convenient size, was then inserted into the uterine cavity and stitched to the cervix by a loop of linen thread. The loop was of sufficient length to allow one end to appear at the vulva when slight traction was exerted on the catheter. Later by cutting one thread the catheter could easily be removed, and further manipulation in the vagina avoided. A control specimen of venous blood, 5 ml., was then taken.

In the two cases of local uterine infection no anæsthetic was necessary, and the catheter similarly secured. The catheter was anchored by adhesive tape to the groin but not to the thigh, thus avoiding any traction. Normal toilet manipulations could then be carried out without disturbing the catheter, and its open end was readily accessible on the lower abdomen for the purpose of injection.

### CONTINUOUS ADMINISTRATION

By this method it was proposed to instil slowly into the uterine cavity a solution of penicillin sufficiently concentrated to enable an adequate amount of penicillin to be brought in contact with the absorbing surface. It will be appreciated that a certain amount of wastage must take place, and that the patient will be lying in a somewhat damp bed. The latter disadvantage can be obviated to a certain extent by placing a thick pad of gamgee below the buttocks. Using a "drip" apparatus, a solution of 500,000 units of penicillin in 500 ml. of normal saline was instilled into the uterus. The rate of administration was set at 30-35 drops per minute. The drip apparatus functioned fairly well and required only, on occasion, a slow "milking" of the catheter to ensure a steady flow. It was intended to instil 500,000 units every six hours, but on the average, depending on the varying rate of the drip, the "course" of 2,000,000 units had been given within twenty hours. The concentration was varied on one occasion, the strength of the penicillin solution being 500 units in 250 ml. of saline. In order to retain the solution as long as possible in contact with the uterine wall, the foot of the bed was elevated on 9-inch blocks. As far as could be ascertained drainage from the uterine cavity was not affected by the

position adopted. Blood specimens, 5 ml., were taken at intervals and tested for bacteriostasis in varying dilutions. (The following table gives a summary of results obtained.)

TABLE  
*Continuous Administration*

Case.	Dilution of Serum-Producing Bacteriostasis.					
	Control.	1 Hour.	2 Hours.	3 Hours.	4 Hours.	20 Hours.
1	1/1	1/1	1/1	1/2	1/1	...
2	Nil	...	...	...	1/1	...
3	Nil	...	...	...	1/1	...
4	1/1	...	...	1/2	...	...
5	Nil	...	...	...	...	1/8
6	1/1	1/1	1/1	...	...	...
7	Nil	1/1	1/1	1/1	...	...

The bacteriostatic test is a standard one employed at the Bacteriology Department of the Edinburgh Royal Infirmary, and is based on the serial dilution method (Fleming). The blood serum in varying dilutions is incubated overnight with a known dilution of a test strain of staphylococcus (the Oxford 5). The dilutions are plated out, and by contrasting the number of colonies grown with a control the degree of bacteriostasis is estimated.

This investigation was directed primarily at determining the absorbability of penicillin from the uterine cavity, and the cases were chosen irrespective of whether pyrexia was present or not. If any pathogenic bacteria were found, however, their sensitivity to penicillin was determined. Attention was directed particularly to the anaerobic streptococcus, and on the one occasion in which it was reported initially as being present, on culture it was rechecked and found to be an enterococcus which was penicillin sensitive. The sensitivity of this particular strain of enterococcus to penicillin is worthy of notice.

#### INTERMITTENT ADMINISTRATION

The catheter was inserted into the uterus in the same fashion as described above. In Cases 8 and 11 (Fig.), penicillin was instilled at three-hourly intervals, and blood specimens taken at varying periods. In Case 9 (Fig.) a large dose of penicillin was instilled at hourly intervals and blood samples taken between each injection. In Case 10 (Fig.), immediately following diagnostic curettage for menorrhagia, a large dose of penicillin was injected directly into the cervix and blood specimens taken at intervals.

#### CASE RECORDS

CASE 1.—Mrs M. H. Age 41. Para 3. Admitted for vaginal bleeding following eight weeks' amenorrhœa. Apyrexial on admission. Remnants of



products of conception removed at operation. Continuous instillation of penicillin 500,000 units in 500 ml. saline. The control blood specimen showed bacteriostasis with undiluted serum. Reference will be made later in the text to this unexpected finding. Blood specimens taken one, two and four hours after commencement of instillation showed bacteriostasis with undiluted serum only. The specimen taken three hours later, however, showed bacteriostasis in a serum dilution of 1 in 2. The swab specimen grew a *Staphylococcus albus* which was penicillin sensitive. The patient remained apyrexial and was discharged seven days later.

CASE 2.—Mrs T. M. Age 26. Para 3. Admitted for vaginal bleeding following twelve weeks' amenorrhœa. Temperature 99° F. Pulse 116 on admission. Products of conception removed digitally from the cervix with subsidence of temperature to 97° F. the following day. There was a rise of temperature of 99° F. on the third day. Continuous instillation of crystalline penicillin 500,000 units in 500 ml. saline. The control blood specimen showed no bacteriostasis with undiluted serum. Blood taken four hours after commencing instillation showed bacteriostasis with undiluted serum only. The temperature dropped eighteen hours later to 97.5° F., and kept at this level for the five days. There was a transient rise of temperature to 99° F. on one occasion only. The swab specimen grew both *Bacillus coli* and enterococci, the latter proving to be penicillin sensitive. She was discharged on the 12th day.

CASE 3.—Mrs A. S. Age 35. Para 6. Admitted for vaginal bleeding following ten weeks' amenorrhœa. Temperature 101° F. Pulse 92 on admission. Products of conception removed at operation. Continuous instillation of 500,000 units of penicillin in 500 ml. saline. The control blood specimen showed no bacteriostasis with undiluted serum. Blood taken four hours after penicillin instillation showed bacteriostasis with undiluted serum. The temperature dropped to 97.5° F. thirty-six hours later and remained at that level. No organisms were grown from the swab specimen. She was discharged ten days later.

CASE 4.—Mrs R. H. Age 23. Para 2. Admitted for bleeding following ten weeks' amenorrhœa. Apyrexial on admission. Remnants of products of conception removed at operation. Continuous instillation of penicillin 500,000 units in 500 ml. normal saline. The control blood specimen showed bacteriostasis with undiluted serum. Blood taken three hours after commencement of instillation showed bacteriostasis in serum diluted 1 in 2. The swab grew an enterococcus insensitive to penicillin. The patient remained apyrexial and was discharged seven days later.

CASE 5.—Mrs C. E. Age 35. Para 2. Admitted with foul smelling vaginal discharge. Temperature 99.5° F. Pulse 100. Treated with sulphadiazine. The temperature subsided twenty-four hours later. Uterus explored seven days later and products of conception removed. Continuous instillation of penicillin 500,000 units in 500 ml. normal saline. The control blood specimen showed no bacteriostasis with undiluted serum. Blood taken twenty hours later showed bacteriostasis in a serum dilution of 1 in 8. No rise in temperature. The swab specimen grew *Bacillus coli*. Patient discharged nine days later. No vaginal discharge.

CASE 6.—Mrs C. O. Age 26. Primigravida. Temperature 102° F. following spontaneous delivery of full term infant. A face delivery after

seventy-one hours in labour. Membranes presumed to have been ruptured for five days. Continuous instillation of penicillin 500,000 units in 500 ml. normal saline was commenced a short while after delivery. The control blood specimen and blood taken one and two hours after commencing instillation showed bacteriostasis with undiluted serum only. The temperature dropped twenty-four hours later to 98.4° F. The swab specimen grew *Bacillus coli*. She remained apyrexial and was discharged nine days later. The uterus was involuting well.

CASE 7.—Mrs J. F. Age 26. Para 3. Admitted for bleeding following ten weeks' amenorrhœa. Apyrexial on admission. Remnants of products of conception were removed at operation. Continuous instillation of penicillin 500,000 units in 250 ml. saline. The control blood specimen showed no bacteriostasis. Blood taken one, two and three hours after commencement of penicillin showed bacteriostasis in neat serum only. The swab specimen grew *Bacillus coli*. The patient remained apyrexial and was discharged twelve days later. The increased concentration of the penicillin solution in this case had evidently not resulted in a like increase in bacteriostatic power of the blood.

#### INTERMITTENT ADMINISTRATION

CASE 8.—Mrs J. H. Age 34. One miscarriage. Irregular temperature since the second day of puerperium following spontaneous delivery of a full term infant. Treated previously for pre-eclamptic toxæmia. Penicillin 200,000 units in 5 ml. of distilled water was injected into the uterine cavity at three-hourly intervals. Distilled water was used as a vehicle to determine its influence, if any, on absorption. The control blood specimen showed no bacteriostasis in undiluted serum. Blood taken half an hour, one hour, two hours, and one hour after the second injection of penicillin showed bacteriostasis in serum dilutions of 1 in 4, 1 in 4, 1 in 2, and 1 in 4 respectively. The temperature dropped to 98.4° F. twenty-four hours later. No growth was obtained from swab culture. She remained apyrexial and was discharged on the thirteenth day of her puerperium. The uterus was involuting well.

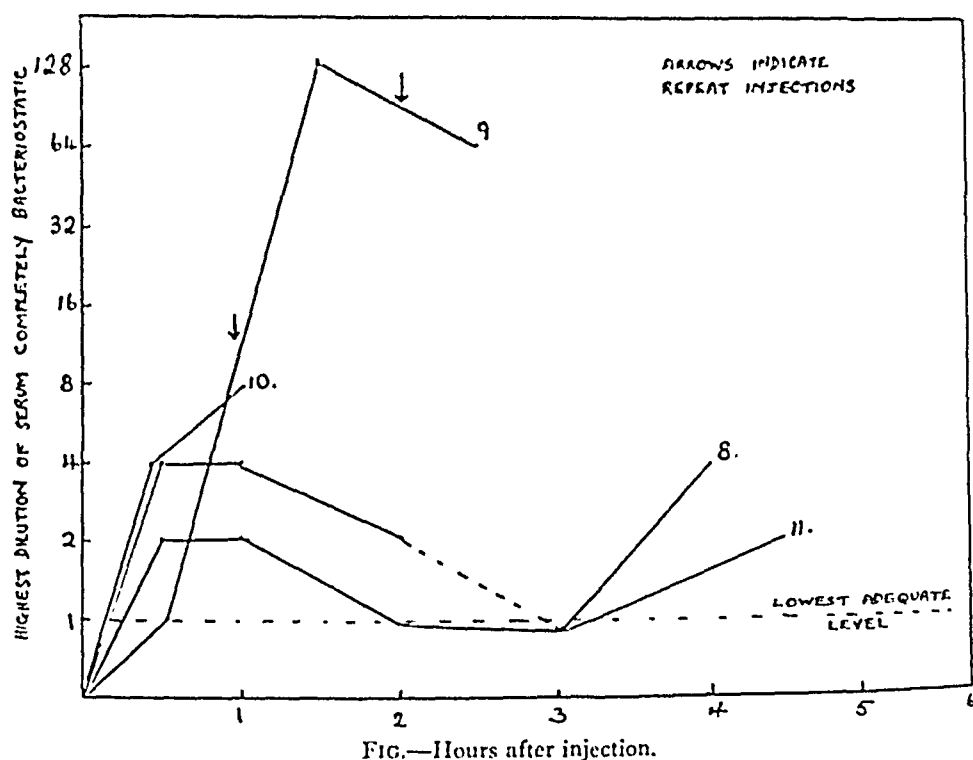
CASE 9.—Mrs J. S. Age 39. Para 4. Admitted for vaginal bleeding following seven weeks' amenorrhœa. Apyrexial on admission. Penicillin 500,000 units in 5 ml. normal saline given at hourly intervals, following operation for removal of products of conception. The control blood specimen showed no bacteriostasis with undiluted serum. Specimens of blood taken half-an-hour after each injection showed bacteriostasis in serum dilutions of 1 in 1, 1 in 128, and 1 in 64 respectively. The swab grew a penicillin sensitive hæmolytic streptococcus (not group A). The patient remained apyrexial and was discharged six days later.

CASE 10.—Mrs J. P. Age 32. Para 1. Admitted for diagnostic curettage for menorrhagia. Following operation 500,000 units of crystalline penicillin in 5 ml. of distilled water were injected directly into the uterine cavity using an ordinary syringe. The control blood specimen showed no bacteriostasis with undiluted serum. Blood taken half-an-hour and one hour after the injection showed bacteriostasis in serum dilutions of 1 in 4 and 1 in 8 respectively. Swab culture was negative.

CASE 11.—Mrs J. R. Age 27. Para 1. Admitted for vaginal bleeding following ten weeks' amenorrhœa. Apyrexial on admission. Penicillin 200,000

units in 5 ml. of saline was injected at three-hourly intervals into the uterine cavity following operation for removal of products of conception. The control blood specimen showed no bacteriostasis and undiluted serum. Blood taken half-an-hour, one hour, two hours and three hours after commencement of penicillin showed bacteriostasis in serum dilutions of 1 in 2, 1 in 2, neat serum and neat serum respectively. A final blood specimen taken some hours later between injections showed bacteriostasis in a serum dilution of 1 in 2. There was partial bacteriostasis in a dilution of 1 in 4. The swab specimen grew *Bacillus coli*. The patient remained afebrile and was discharged five days later.

#### INTERMITTENT ADMINISTRATION



#### RESULTS

It will be seen, therefore, that bacteriostatic levels of penicillin have been obtained in the blood by both methods. With the continuous method it was possible to obtain bacteriostatic levels by diluting the serum 1 in 2. In Case 6 (the septic abortion) a high bacteriostatic level was obtained, the serum still producing bacteriostasis in a dilution of 1 in 8. Florey and Heatley have pointed out that a more prolonged effect is produced when penicillin is injected into an infected cavity, and one may assume that a similar effect was exerted here. A further observation requiring explanation is the presence of bacteriostatic levels in undiluted serum in three control specimens Cases 1, 4 and 6. A study of the bactericidal power of the blood during pregnancy (Miller and Whitaker) showed that there was a gradual increase of the bactericidal activity of the blood, reaching its maximum at or about the time of delivery. This might offer the possible explanation in these cases.

It has already been pointed out that the continuous method of administration had considerable drawbacks, and it is evident that the bacteriostatic levels obtained are not sufficiently high to produce a sustained therapeutic level of penicillin in the blood.

The results obtained by intermittent injection, however, are most encouraging, the lowest blood level being a serum dilution of 1 in 2, and the highest, the enormous concentration in the blood of a serum capable of being diluted 128 times and still producing effective bacteriostasis (Fig.).

In comparison with the bacteriostatic results achieved after a single intramuscular injection of penicillin (McAdam *et al.*), 10,000 units produced a concentration in the blood sufficient to maintain bacteriostasis when the serum was diluted 1 in 2, 15,000 maintained bacteriostasis with a serum dilution of 1 in 4 and 100,000 units maintained bacteriostasis when the serum was diluted 1 in 128.

It would appear, therefore, that penicillin, when instilled into the uterine cavity is capable of being absorbed into the general circulation and thus must exert an adequate local concentration in the uterine wall and in the channels draining the organ, namely the lymphatics and pelvic veins. For preference, the method of injection is by intermittent instillation for reasons already mentioned. An effective dose recommended is 200,000 units of penicillin in 5 ml. of normal saline or distilled water injected at three-hourly intervals.

It is now proposed to discuss its clinical application.

### THERAPEUTIC USE

The septicæmic varieties of penicillin sensitive bacteria respond readily to intramuscular injections of penicillin, but it is with the invaders of the genital tract which produce a local effect that this method of administration might prove to be of value. The Gram-negative bacteria do not respond to systemic administration of penicillin in the vast majority of cases, and it would appear that no useful effect could be obtained here. This objection, however, is not without reservations, for Fleming states "that some bacteria, classed as insensitive bacteria, which although insensitive to penicillin in concentrations which by systemic administration can be reached in the blood, are yet sensitive to the higher concentrations with which they may come in contact, when penicillin is applied locally."

Up to the present in this small series of cases no infection, post-abortion or puerperal, due to the anaerobic streptococcus has been met with, but it is hoped that this type of infection might respond readily to local administration of penicillin.

Gibberd quotes: "It must be remembered that the problem of therapy in severe anaerobic infections is bound up with the problem of killing bacteria in the midst of relatively large blood clots in the larger pelvic veins and abdominal veins. From their very position these

organisms are likely to be inaccessible to bacterial substances in the general circulation." Kenny writes that the hopes of obstetricians are raised by reports of sensitivity of anaerobic streptococci to penicillin in vitro, but quotes from a communication from Cruikshank that although cases of septicæmic varieties of the anaerobic streptococci have been treated with penicillin systemically, no luck had resulted, apart from a finding at autopsy that the primary septic thrombophlebitis had cleared up. Penicillin given locally may provide the possible answer to this problem.

The success of systemic penicillin therapy in moderately severe post-abortal puerperal infection with *Clostridium welchii* infection is reported (Goldberg and Konigsberg). It is suggested that the local application of penicillin in such cases would also be of extreme benefit if not more speedily efficacious.

### PROPHYLACTIC USE

Although prevention of puerperal sepsis by aseptic and antiseptic methods are the chief means of guarding against infection, nevertheless certain types of cases such as the "failed forceps", prolonged labour when the membranes have been ruptured for some time, and manual removal of the placenta, are instances where penicillin instilled by this route might be of benefit. In septic abortions where concern might be felt at emptying the uterus, evacuation, followed by local penicillin immediately, may prevent any unwelcome sequelæ.

### ADVANTAGES

Penicillin is not inactivated in the presence of blood or pus. Intermittent local therapy can be carried out for long periods without subjecting the patient to painful and frequent injections.

It is also possible that its suspension in an oily medium might produce a prolonged effect. It can be used in any strength without toxic effect.

### PROBABLE DISADVANTAGES

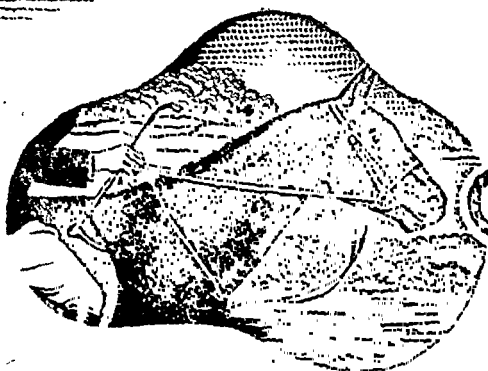
Penicillin has been shown to have a retarding action on blood clotting (Fleming and Fish), but no undue bleeding was observed in any of the cases treated.

### SUMMARY

Penicillin is absorbed from the uterine cavity and produces effective bacteriostatic levels in the blood stream.

Two methods of administration were employed, continuous instillation and intermittent injection, the latter being the preferable method.

Suggestions as to its clinical application have been made.



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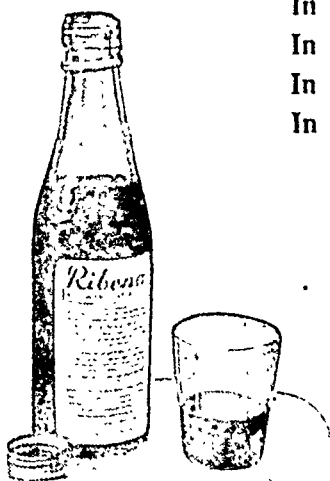
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## ACKNOWLEDGMENTS

I wish to thank Dr E. Chalmers Fahmy for allowing me to carry out this investigation on the cases in his wards and for his encouragement throughout. I am indebted to Mr J. Dick, technician to the Bacteriology Department of the Edinburgh Royal Infirmary, for undertaking the bacteriological and bacteriostatic investigations, and not least to the nursing staff for their willing co-operation.

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## HÆMORRHAGE IN OBSTETRICS: THE RELATION BETWEEN THE GENERAL PRACTITIONER AND EMERGENCY SERVICES \*

By RICHARD DE SOLDENHOFF, M.B., F.R.C.S.Ed., M.R.C.O.G.

HÆMORRHAGE in obstetrics is a very broad field, but narrower when emergency services are concerned with it. The main function of the service in Ayrshire is, as Stabler found in the Newcastle district, the resuscitation of cases of post-partum hæmorrhage and incomplete abortion with which I intend mainly to deal. The ancients had no emergency service, but they were fully cognisant of these main causes of obstetrical hæmorrhage. Hippocrates in *De Superfætatione*, 460 years before the Christian Era, had already advocated, in cases of a dead baby with retained placenta, weight traction. His method consisted of seating the patient on a high stool with the child resting on a bundle of newly plucked wool, or he had two bladders filled with water and covered with wool, these being pricked, and as they gently subsided the baby's weight would gradually draw the placenta out. He goes on to say if the navel string be broken then the proper weights must be tied to it. Both he and Celsus, who lived in the time of the Emperor Tiberius, would appear to have had no fear of manual removal of the placenta. Their methods read very similarly to those described in more modern journals and textbooks. Aetius in the fifth century realised the danger of overcoming a uterine contraction ring by force when endeavouring to reach the placenta. He stresses the need to desist rather than cause excessive "fatigue." This word evidently is a precursor of the modern term "obstetric shock." They also realised that a placenta could undergo autolysis and come away in the lochia without harm to the patient. Eucharius Rhodion, or Rösslin in 1532 in Germany, speaks of manual removal for post-partum hæmorrhage, and most of the older writers mention traction on the cord in delivery of the placenta but condemn it in hæmorrhage, and Ambroise Paré in the sixteenth century must have been the modern of his day as he advised immediate manual removal of the placenta after every delivery. These authors had no weapons against puerperal sepsis, and unfortunately have left no statistical reviews of their cases, but from their writings it is obvious that puerperal morbidity was high. Smellie in the eighteenth century gives a description of management of the third stage and post-partum hæmorrhage which is a delight to read, and his description of manual removal of the placenta might well be incorporated in every modern textbook. He stresses the need for deliberate and slow extraction of the child, which gives the uterus time to contract down as its contents are evacuated. He advocated that the

\* A Paper read to the Edinburgh Obstetrical Society, 10th March 1948.

cord be left to drip after removal of the baby so as to diminish the placental volume, that there be no interference with the fundus of the uterus, and that gentle traction on the cord aided by the mother's own expulsive efforts should be enough; but if there was hæmorrhage manual removal should be attempted. He stressed how interference without indication is apt to excite irregular contractions, and lead to irregular separation of the placenta and hæmorrhage. McClintock, who edited an edition of Smellie's book, had anticipated our American colleagues by over one hundred years, by giving liquid extract of ergot before delivery of the child when the cervix was fully dilated, and no obstruction to delivery. He stated this cut third stage loss, but mentioned the same drawback as is found nowadays, the occasional retention of a placenta by a contraction ring. Professor Alexander Simpson wrote about subcutaneous injection of ergot in the *Edinburgh Monthly Journal* of 1876, and said the hypodermic syringe would be indispensable in every obstetric bag. How little he knew that the medical world would be the slave of the syringe in the future.

TABLE I

*Quinquennial Rates per 100,000 Live Births (1945 Report)  
By Cause of Death*

	1931-35.	1936-40.	1941-45.
Abortion (non-septic) . . . .	14	16	12
Placenta prævia . . . .	29	20	12
Accidental hæmorrhage . . . .	24	21	14
Other puerperal hæmorrhage . .	40	41	39
Puerperal sepsis . . . .	215	120	71

Maternal mortality has shown a steady downward trend in the last ten years, the most dramatic fall being in puerperal sepsis. Hæmorrhage has not fallen to the same extent though the figures of placenta prævia and accidental hæmorrhage would appear to show a slight drop. Post-partum hæmorrhage, however, has varied very little and still accounts for over 50 per cent. of the deaths from hæmorrhage. In the figures for 1947 (by courtesy of the Registrar-General of England), of 194 deaths from "hæmorrhages in childbirth," 117 or nearly 60 per cent. were due to post-partum hæmorrhage. Similarly, in Scotland (by courtesy of the Department of Health for Scotland), more than 60 per cent. of the deaths from hæmorrhage in 1946 were due to post-partum hæmorrhage, and in 1947 55 per cent. I have had the privilege of seeing the Department of Health for Scotland Maternal Death Forms for 1946 and 1947 dealing with fatal hæmorrhage. These by no means represent all the deaths occurring from hæmorrhage, as the filling of these forms is not compulsory. To my mind this is a great pity. They make tragic and salutary reading, and before I make any remarks about them I might say I have filled in my share of these forms. Post-

partum hæmorrhage is stated (De Lee-Greenhill, 1947) to occur in 1 to 5 per cent. of deliveries. In my own maternity unit the incidence is 3·5 per cent. It would appear that 50 to 60 per cent. of deaths from post-partum hæmorrhage are avoidable (McCormick, 1947), and on looking at my own maternal deaths from post-partum hæmorrhage in a cold and reflective light I must agree with this. There were 99 deaths from hæmorrhage accounted for by the Department of Health forms and 67 per cent. of them were due to post-partum hæmorrhage, and it would appear that 50 per cent. at least were avoidable. It is tragic to think that nearly 40 per cent. were young women pregnant for the first time. Most of these women died in hospitals. Why? Because they were moved there after delivery of the child. It is interesting to note that in 22 per cent. of these cases Credé's expression of the placenta had been admittedly used, and I would go further and say that in almost 100 per cent. there had been manipulation of the fundus of the uterus.

What relation has all this to the emergency services? In the vast majority of these cases help had been summoned, but generally too late. Another interesting point is that death was attributed to obstetric shock in nearly 40 per cent. of cases, but in most of these cases post-partum hæmorrhage had been a factor. The term obstetric shock appears to be a protective umbrella under which one is apt to shelter from culpability. In only a small number of cases was post-mortem examination carried out.

The assessment of the degree of shock and hæmorrhage is most important, as I am certain in the past a large number of cases had been over-transfused. The pure cases of hæmorrhage stand massive transfusion well. The cases complicated by shock do not benefit to the same extent and are apt to develop cardiac failure from over-transfusion. Here I am speaking from personal experience as I have seen this type of case die of heart failure purely from over-transfusion. One must not treat the average woman suffering from post-partum hæmorrhage and shock as one would treat a fit soldier who has been wounded and requires transfusion.

Many of these cases, as well as their post-partum hæmorrhage, have had operative deliveries, Credé's expression of the placenta, and other physical manœuvres conducive to shock, and they are not simple problems in resuscitation. After replacement of blood loss, further treatment often requires the exhibition of morphia. It is necessary strictly to avoid overheating the patient. Operative intervention is better delayed until the patient rallies, but if it be essential to operate during shock I myself favour the use of methedrine temporarily to raise the blood pressure.

Dr W. I. C. Morris, who was Consultant Obstetrician to Ayr County Council before me, started an Emergency Domicillary Obstetrical Service in 1937 in Ayrshire, and delivered a paper to this Society in 1939 concerning the work done. His foundation still carries the

main structure of the Service and, as in all buildings where the foundations are firm, structural changes have not diminished its value. I will not recapitulate the contents of the equipment; the lantern slide shows the whole outfit that is now used. The biggest change, as you see from the comparison of the figures of the work done in 1937-38 and in 1947, concerns the increase in cases of hæmorrhage and the decrease in operative obstetric work (Table II).

TABLE II  
*District Cases*

	1937-38.	1947.
Post-partum hæmorrhage . . . . .	26	32
Abortions . . . . .	10	24
Ante-partum hæmorrhage—accidental . . . . .	4	9
Ectopic gestation . . . . .	1	1
Operative delivery . . . . .	43	2
Perineal lacerations . . . . .	7	...
Cardiac failure . . . . .	1	...
	<u>92</u>	<u>68</u>

Since 1937 there has been a great improvement in Transfusion Service, and now plasma and Group O Rh positive and, when available, Rh negative blood are carried. Since the war there has been a considerable falling off in blood donors, and we find it essential to get blood from the relatives as quickly as possible after the patients have been revived, as gratitude very quickly blows cold. Consequently we carry with us simple equipment for taking blood and this is returned to Glasgow to the West of Scotland Blood Transfusion Service.

TABLE III  
*District Emergency Service, 1947*  
*Pints of Blood and Plasma used*

Type of Case.	Blood.	Plasma.
Post-partum hæmorrhage . . . . .	26	17
Abortion . . . . .	18	12
Ante-partum hæmorrhage . . . . .	7	7
Ectopic . . . . .	1	1
Total . . . . .	52	37

During last year, as seen in the table, a considerable quantity of blood and plasma was used, naturally mostly for cases of post-partum hæmorrhage. We endeavour to give Rh compatible blood whenever possible, and we carry a high titre testing serum to pick out the Rh positive patients. Admittedly, this is not 100 per cent. accurate in emergency, but its use certainly means that the number of incompatible transfusions and the future immunisation of Rh negative mothers with Rh positive blood will be lessened.

The equipment contains everything necessary to deal with cases of

post-partum hæmorrhage and abortion. It goes out nowadays in a small 8 h.p. car with one of the senior staff and a resident. On receipt of a call the team sets out and the case is dealt with on its merits. As cases of post-partum hæmorrhage constitute the majority, I will deal with what I consider the most important points in their treatment, and particularly how the general practitioner and the service should co-operate.

First, I do not think the Emergency Services are summoned early enough. The vast majority of practitioners appear to have no clear-cut plan of campaign when they meet with one of these crises. Their first reaction, I think, in abortion or post-partum hæmorrhage, from the study of the Department of Health Maternal Death Forms, is an attempt to express the placenta in both cases by vigorous squeezing and pushing of the uterus. I would heartily condemn this. In the vast majority of cases the hæmorrhage is associated with retained products, and the quickest way to control this hæmorrhage is by their removal. I think the bogey of manual removal of the placenta under thirty minutes to one hour after delivery must be, once and for all, destroyed. To my mind the bogey is after this time, and when the patient has lost blood. I have had such bitter lessons that I now insist in my Maternity Unit of 103 beds with 3 house surgeons and a registrar, that each new resident within the first week of his arrival must do a manual removal of the placenta with my guidance. I am frank about this; it is in a case of a forceps delivery and the only indication here is to instruct the resident. I believe that within the immediate period after delivery the only danger is of a morbid puerperium and nowadays with the asepsis at our command and the chemotherapy this danger is minimal.

I would go further and say that I think that, in the future, no practitioner intending to undertake midwifery should leave his teaching school without having done a manual removal of the placenta.

In the past year, 82 cases under my care have had this operation. In the 49 cases in which it was carried out within the first hour not one died. Of the remaining 33, two died. The fatal cases were:—

(a) An elderly multipara with a bad obstetric history, in whom atonic hæmorrhage occurred immediately after delivery, precious time being wasted in attempts to start blood transfusion and to control the fundus by abdominal massage instead of proceeding at once to manual removal of the placenta.

(b) A severe case of pre-eclampsia in which a comparatively slow but continuous hæmorrhage, spread over a third stage lasting more than two hours, led to severe collapse.

In both these cases the placenta was removed too late and the patients died despite blood transfusion. They point their own lesson and remedy.

Of the cases in which the placenta was retained more than one hour, 58 per cent. were retained less than four hours and 12 per cent.

were retained over eight hours. In one case the third stage was allowed to continue for ninety-three hours, until the patient, no longer actually bleeding, had rallied from collapse associated with an accidental ante-partum hæmorrhage of toxæmic type. Her systolic blood pressure remained between 80 mm. and 90 mm. of mercury for seventy-two hours. When it reached 100 mm. the placenta was easily removed manually without hæmorrhage.

No woman who has had a previous history of retained placenta and post-partum hæmorrhage should be delivered at home, and no woman who has had a difficult operative delivery should be allowed to retain her placenta after delivery—the margin of safety is too small. She is a candidate for shock, and if there is hæmorrhage she may suddenly become a case requiring difficult resuscitative measures.

I will never forget one of my first emergency calls in Ayrshire. I was called to a nursing home there to be greeted by, I think, the very prototype of Francis Brett Young's "Dr Bradley," and as I walked into the bedroom he came towards me with his bared hand and arm to the elbow covered with blood and said, "I just had to put my hand in Doctor and take the placenta out as she was bleeding." This practitioner qualified in 1893 and is sufficiently old to have remembered the precepts of his masters. That woman did extremely well.

Nobody gives a better description of manual removal of the placenta than Smellie, and his method has recently been hailed again in the journals as an original discovery. An anæsthetic within the first thirty minutes is not essential. To my mind there is one reason only for manual removal of the placenta and that is hæmorrhage in the third stage. I am prepared to leave the placenta for many hours so long as there is no blood loss. Some of you will say, "What about those cases who revive from a condition of shock immediately the placenta is removed and there has only been a moderate hæmorrhage?" In my experience these uteri have always been irritated by interference through the abdominal wall and the placenta is partially separated and gripped by the cervical canal. A similar occurrence takes place, in incomplete abortions, and the patients recover dramatically once the placenta has been removed. This condition is quickly appreciated by a vaginal examination. I would strongly deprecate forcing a way through a contraction ring to a placenta in the body of the uterus unless there is hæmorrhage. Recently the Hippocratic method of weight traction has been revived and, in hospital, I have found it quite useful in selected cases. It does not disturb the patient, and as long as there is no bleeding I have left the weight on for twenty-four hours and it has worked well. In so many of the cases we go out to they are shocked from a violent Credé's manœuvre and are still bleeding. It is our practice to revive them with blood, and as soon as a sufficient volume has been replaced, endeavour to raise the blood pressure with methedrine and remove the placenta.

If a woman is still bleeding while she is being transfused, and not

recovering, no time is wasted and the placenta is removed, if necessary without an anæsthetic.

In cases of abortion in the home, where there has been considerable blood loss, an attempt is made to replace it, to bring back the patient's blood pressure, and then to evacuate the contents of the uterus. I concur heartily with Stalworthy that the sooner an incomplete abortion is evacuated the less danger there is to the woman from hæmorrhage and the quicker her convalescence. For anæsthesia I use pentothal sodium.

Of 14 cases of abortion given pentothal, 11 required less than .4 gram. Two cases of abortion initially treated at home died later in hospital. I consider that the ambulance journey played a significant part in these patients' deaths (Table IV).

TABLE IV

*Deaths*

1. Post-partum hæmorrhage. (Moribund.)
2. Accidental hæmorrhage. (Moribund.)
3. Post-partum hæmorrhage. (Manual removal of placenta.)
4. Abortion. (Died in hospital.)
5. Septic abortion. (Died in hospital.)

I will not have any patient moved to hospital with an abortion if there is the slightest doubt about her condition. Curettage in the home with the emergency equipment is simple and life-saving. Similarly, with cases of post-partum hæmorrhage, they must be treated in the home. Where it is essential to bring cases of placenta prævia and accidental hæmorrhage into hospital, their condition must be improved as much as possible before removal and I have no scruples in using vaginal packs if I consider them necessary. They can play a life-saving part.

The sphygmomanometer has an important part to play in these cases, but one cannot be guided entirely by it, as trying to force a blood pressure up in obstetrically shocked cases by large volumes of blood and plasma can be a fatal procedure. I myself have had patients whose blood pressure has been below 80 mm. of mercury systolic for more than three days and who have recovered, and I am sure this experience can be paralleled by many others. It is, however, of vital importance in estimating the chances of these women to travel safely. I will not have moved by ambulance any distance a patient whose blood pressure is below 90 mm. Hg., and I prefer them to be above 100 mm. Hg. The obstetrically ill patient, as I mentioned before, does not react like the wounded soldier.

As hæmorrhage in the first and last chapters of pregnancy has taken up a considerable part of my time in the battle against maternal mortality, I might be allowed the impertinence of some suggestions.

I work in the most intimate contact with my obstetric patients and am virtually on call twenty-four hours a day, eleven months in the year.

Consequently, in a large unit like mine I get a concentration of obstetrical horrors. Though one must be ever on guard against calamity, one must preserve a sense of proportion and realise that the majority of deliveries are normal. Many general practitioners make the proud boast that they have never had a mother die, or perhaps only one in a lifetime of practice. Unfortunately, the staff of a hospital cannot echo this : some of the deaths occurring in hospital are booked cases, but a larger proportion of them start off as emergencies outside.

There is often delay in midwife-attended cases between the doctor being summoned (he is often out on another case), his arrival, his attempt to stop hæmorrhage, and then the call for the emergency team. I would suggest that the midwife have authority to send to the hospital for help at the same time as she summons her own practitioner.

In the case where the practitioner finds the patient too shocked for manual removal of the placenta, there should be no hesitation in giving ergometrine either intravenously or intramuscularly. It may control the hæmorrhage temporarily. I would also like to see the practitioner, when there is a severe post-partum hæmorrhage, do an immediate manual removal of the placenta. He should not be doing obstetrics if he cannot do it. As I mentioned, the optimum time for manual removal in a bleeding patient is within a short period of delivery. The risk is then minimal ; it is the late removal that is fraught with danger. Most deliveries occur without trouble and these heroics should be rarely necessary.

There are many cases of post-partum hæmorrhage which never reach hospital, and their legacy is a long convalescence from a severe anæmia. Would not they have been better with a blood transfusion at the time and a more rapid return to normal health ?

I am certain that some cases of post-partum hæmorrhage are caused by Credé's expression and using the uterus as a piston to push the placenta out. In the third stage I think the less interference the better, if there is no advance of the placenta with gentle traction on the cord and the mother's own expulsive efforts and no bleeding, then everything should be left until placental separation is evident.

Intravenous ergometrine before delivery of the child is not a good thing in domiciliary midwifery, owing to the occasional case of contraction ring and then the necessity, if there is hæmorrhage, for manual removal of the placenta under general anæsthesia.

It is difficult to convince practitioners that there is no necessity to examine cases of ante-partum hæmorrhage in the home, as they are still kept after two or three warning hæmorrhages before being sent into hospital. All hospitals will take cases of ante-partum hæmorrhage without question, the examination of the patient is carried out like a religious rite, and even then hæmorrhage may start dramatically and be difficult to control. Once a patient is disproved a placenta prævia she can be sent home if there are no symptoms suggestive of toxæmia, and beds are not wastefully used. If examination is required in the



home it must be that it is forced on the practitioner by lack of specialist service, great distance from a hospital, or adverse weather conditions. The doctor must then be prepared to carry on after his examination. If the patient bleeds he must pack the vagina tightly, rupture the membranes, or bring down a leg, depending on circumstances. I look upon vaginal examination of a case of ante-partum hæmorrhage outside hospital simply to make a diagnosis, as criminal.

In incomplete abortions where there is any bleeding I would stress the need for immediate hospitalisation and curetting (Stallworthy). Waiting to see whether it will complete itself is likely to impair the patient's future health and cause longer hospitalisation as well. Last year we had 351 admissions for abortion, and it was rare for any to stay in hospital more than three days. The only treatment I would advise in the home is morphia and ergometrine, and no effort should be made to express any retained products as this can be as shocking in these cases as in post-partum hæmorrhage.

The earlier the emergency service is called in to a case, the quicker it will be finished and less blood will be used. It is the delayed case that causes anxiety where the difficulty arises in striking the happy medium between blood replacement and overloading of the circulation. It must be remembered that more so in obstetrics than in anything else stereotyped treatment must be avoided. Each case is essentially different, which is perhaps the fascination of obstetrics. These remarks are made with a sincere desire to reduce the figures from hæmorrhage in maternal mortality, and the conclusions are the distilled essence of much bitter thought over cases of this type at which I have been a contributory factor in their demise, along with the hæmorrhage. I would plead for post-mortem examinations on all these cases as I am sure, particularly where there is an element of shock, it is not unlikely as De Lee states, that there has been an undiagnosed rupture of the uterus extending from the cervix.

Finally, there should be a conference over every maternal death either in hospital or outside, and all interested should be present at the discussion. It is by doing this that future tragedies can be avoided. To err is human, and confession of errors makes them more likely to be avoided in the future.

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## DISCUSSION

*Dr Sturrock* said he agreed in general with Dr de Soldenhoff's views. If cases of incomplete abortion were evacuated by operative methods as soon as possible the morbidity was reduced, and the incidence of sterility diminished. The chief barrier to this was the difficulty in securing an adequate number of hospital beds for such cases.

Cases of antepartum hæmorrhage were best dealt with in hospital if such facilities were available, and no exploration of the lower uterine segment should be made unless there was present someone capable of dealing with the case should placenta prævia be discovered. In third stage hæmorrhage every doctor practising midwifery should be able and willing to carry out manual removal of the placenta. If this were done early rather than late the risk to the patient was greatly reduced.

In regard to the criticism of Credé's manoeuvre, Dr Sturrock thought it important to differentiate between the classical Credé procedure and the use commonly made of the empty uterus as a piston to expel an already separated placenta. At the same time he admitted that the signs of placental separation, though clearly definable in theory, were not always as easy to recognise in practice, especially in stout patients. Yet a classical Credé's expression of the placenta was often successful if performed under anæsthesia with, in the event of failure, preparation made for proceeding forthwith to manual removal.

Dr Sturrock added that although blood transfusion was a life-saving factor, it was disturbing to note that in their own Maternity Hospital Report for 1946 they had had three deaths from transfusion reactions. He thought some patients were merely transferred from one death list to another. The recognition of blood incompatibility still required clarification.

*Dr Davidson* said that on several occasions he had had to remove a placenta manually, and in the single case in which serious collapse had resulted, he attributed this to delay in undertaking the operation. He wondered what proportion of retained placentas were of the truly adherent type and how many were simply not expelled. The removal of an adherent placenta was not an easy procedure, but he agreed that it was one that any doctor doing midwifery should be able to carry out.

*Dr Alison Ritchie* said she would like to know whether she were right in thinking Dr de Soldenhoff had said that an anæsthetic was not necessary during the first thirty minutes.

*Dr Morris* said Dr de Soldenhoff had made reference to him in connection with the initiation of the Ayrshire Emergency Service. It was interesting to note how the service had altered in ten years. At initiation it was a general emergency service, and, in the first report, cases of difficult delivery comprised the majority. That side of the work had now dropped out completely. He himself had decided it was not worth the trouble and the additional risk, and he thought Dr de Soldenhoff was right to confine his service to cases of hæmorrhage.

He thought all must have been struck by the extraordinary incidence of obstetric disasters which Dr de Soldenhoff had described. In Edinburgh, where the bulk of obstetrical practice was drawn from within ten miles of the hospital, it might be difficult to realise how in the country these cases became

rapidly serious. Whether the population was inherently a much less healthy one than the population of Edinburgh he could not say.

Personally in his own period of service in Ayrshire he had only on one occasion had to pack a vagina, and this was in hospital on account of having hæmorrhage arising as a result of incautious examination of a case of placenta prævia. He had never had to pack a patient outside hospital, and he was not convinced that vaginal packing should be taught as a treatment of election for the general practitioner. It might occasionally be necessary to apply a temporary tamponade. Direct pressure over the cervix with the clenched fist in the vagina for a matter of ten minutes would arrest most acute hæmorrhage in placenta prævia.

Dr Morris noted that Dr de Soldenhoff did not advocate the removal of the placenta on a strict time basis in the absence of hæmorrhage. He himself felt that if the placenta had been in the uterus for an hour or more, the patient was in danger of hæmorrhage at any moment and he would prefer to remove the placenta before hæmorrhage occurred. He described a case of constriction ring in the third stage when it was impossible to introduce more than two fingers into the uterus. Following the intravenous administration of 15 mil. of 20 per cent. magnesium sulphate, when complete relaxation of the ring took place he was able to separate the placenta easily. Fearing too great a degree of relaxation, he had had the patient given a further intravenous injection of 5 mil. 10 per cent. calcium gluconate when immediately the ring closed down upon his wrist to such an extent that it was extremely difficult to withdraw his hand.

Dr Morris said he agreed that obstetrical teachers had overstressed the dangers of sepsis following manual removal of the placenta and for many years now he had entirely neglected the elaborate aseptic ritual at one time practised in the Simpson Memorial Hospital. Nowadays he deliberately refused to put on a gown at all as it was no protection to the patient when the sleeve was completely soaked with blood. He advocated the wearing of gloves with the application of Dettol cream from wrist to elbow on the bare forearm. The patient should be lying on her back. There was no need to adopt the lithotomy position, and sterilised drapings were unnecessary provided a good antiseptic technique was employed.

*Professor Kellar* said he would like to pay tribute to Dr de Soldenhoff's profound reading of the history of manual removal of the placenta. He had referred to Smellie, but perhaps he might have mentioned that it was William Hunter a few years later who had said that early removal of the placenta was wrong and advocated delayed technique. Denman had endeavoured to reconcile the two methods, and had advocated what was substantially the present-day management.

Dr de Soldenhoff had mentioned the danger of over-transfusion, and Professor Kellar said he took it that he meant over-transfusion of blood. They had had one or two mishaps with plasma transfusion, associated with suprarenal hæmorrhages, which indicated that it might be equally dangerous.

*Dr J. A. Chalmers* said he would like to mention the immediate use of morphine in obstetrical collapse. He had found that in those cases where it had been given the condition of the patient was much better than in those who had not had it. He advocated the use of amyl nitrate inhalation in retained

placenta due to constriction ring. It avoided the risk of a flaccid uterus following the relaxation of the ring, owing to its transient action.

In regard to transfusion accidents, the only serious mischances he had seen here were in the patients who had been overloaded with plasma. If there was delay in obtaining blood he felt that saline should be used, as this could be cleared from the circulation rapidly and replaced with blood when it was available.

*Dr Macgregor* said that he thought the dangers of the vaginal pack had been exaggerated. He himself believed that it was not justifiable to move a patient to hospital after a severe hæmorrhage and while she was still bleeding. In his experience arrest of such bleeding could be obtained by efficient packing. He himself would not take the risk of sending such a patient a long ambulance journey of say sixty or seventy miles unless the vagina had been packed.

He agreed with *Dr de Soldenhoff* that if there was any undue hæmorrhage after delivery of the child, it was advisable to remove the placenta manually rather than let the bleeding trickle on. It was just such slight hæmorrhage continuing which was deceptive; it was much better to carry out a manual removal of the placenta while the patient's condition was good than to wait until this procedure became imperative on account of the deterioration of the patient's condition.

*Dr Alexander* said he regretted there were not more general practitioners present to comment on the points *Dr de Soldenhoff* had raised. He himself felt apprehensive regarding manual removal of the placenta. As a resident he used to remove placentas not infrequently, and in country practice occasionally. But after years with no such emergencies he wondered whether he ought to undertake this operation, especially where he could get skilled assistance relatively easily. In any cases that he had had in the last ten or fifteen years he had called in a consultant, and he wondered if he were shirking his responsibilities in view of what had been said. *Dr Alexander* said he thought the doctors in Ayrshire should be felicitated in having at their service such excellent arrangements for these anxious cases.

He was reassured to hear *Dr de Soldenhoff's* recommendations in regard to incomplete abortions. He agreed that the wisest thing was to give the patient morphia if necessary and send her into hospital without delay.

*Dr Somerville* said he would not call himself in any way an expert in removing placentas, and he shuddered to think of himself doing this. It sounded very easy but he sometimes wondered whether he should give up all such practical work. In placenta prævia, with the ambulance service they had in the country, he was very chary of sending the patient to hospital without doing something to prevent further bleeding, so he would like a further word of guidance in regard to the use of the pack in antepartum hæmorrhages.

*The President* said the question of hæmorrhage was a very important one. Statistics showed that the number of deaths from sepsis and toxæmias had fallen in the last few years, but those from hæmorrhage cases had remained almost stationary and showed a higher proportion compared with the two other main causes. He liked *Dr de Soldenhoff's* practice of taking blood from a relative to make up for the blood he was using for a transfusion. This was carried out in many hospitals in America and was of great benefit to the blood transfusion service. The President also considered that manual removal of

the placenta at the time of a difficult obstetric delivery was an excellent one, and although it might be considered by many present to be novel, he remembered that Dr Haig Ferguson frequently carried it out. He, like Dr Morris, also wondered why Dr de Soldenhoff left the placenta *in situ* indefinitely if there was no bleeding. He would not have thought there would be any risk in removing a placenta, bleeding or no bleeding, within an hour after delivery, and he himself adopted such treatment.

The President said he agreed with Dr Morris that elaborate aseptic technique was unnecessary for manual removal of the placenta in an emergency. He himself dispensed with gloves, feeling that the bare hand was more sensitive and made it easier to strike the correct plane. There was always great controversy on the subject of packing, but he entirely agreed with Dr MacGregor and taught his students that if there was profuse bleeding in an antepartum hæmorrhage the vagina must be packed if the journey to hospital was of any great distance. He demonstrated to them how to use the old-fashioned kite-tail pack, which he considered the most easy to insert under domiciliary conditions. The dangers of sepsis had been greatly over-exaggerated; in Dr Sturrock's statistics presented to the Society last session only one of the cases who had been packed had died, all the others having done well. He considered it much wiser not to risk the patient's life by the possibility of a severe hæmorrhage in transit but to take the lesser risk of possible infection, which if it occurred nowadays usually yielded satisfactorily to treatment.

*Dr de Soldenhoff*, replying, agreed that unfortunate transfusion reactions contributed to fatal issues. Blood compatibility could generally be avoided, provided a high titre anti-Rh serum was available, but, even with this advantage and with direct cross-matching, occasional disasters were possible. He was very frightened now of plasma. Wonderful in the case of the wounded healthy male, it was not nearly so wonderful in the case of the unhappy, shocked female, and he now gave blood rather than plasma whenever possible. He had seen several cases of suprarenal hæmorrhage peculiarly coincident with the giving of plasma.

Dr Ritchie had asked about anæsthetics. Sodium thiopentone was a very suitable anæsthetic for emergency service work, used in minimal doses. In hospital he preferred gas and oxygen. Dr de Soldenhoff said he did not remove the placenta without an anæsthetic as a routine, but he considered it justifiable to do so in the face of urgent and potentially disastrous third stage bleeding.

To Dr Alexander he would say that one should always be able to remove a placenta, having once done so and got over the initial fear. It was a terrifying experience for a house surgeon to remove his first placenta; he did not know at all what he was going to find, but having once removed one under supervision he was capable of doing any other in an emergency. He said he was certain it was the initial fear that was the cause of so many tragedies seen.

Dr Morris was rather against leaving the placenta in for any length of time, and wherever there was any hæmorrhage he agreed with him. At the same time it was interesting in cases of retained placenta without hæmorrhage to note how many had either the cervix contracted down or a constriction ring below the placenta, and it was his contention that it was very dangerous to force a way through these rings.

Regarding the controversial subject mentioned by Dr MacGregor, the advisability or otherwise of packing, he agreed again with Dr Morris that it

was a shocking procedure and not always an easy one to carry out. Like Dr Morris, he had used it in hospital when examining a patient. On the other hand, a patient who had a sixty-mile journey to go to hospital might perhaps be packed with advantage—it might mean death if she were not packed.

Dr de Soldenhoff said he was sorry that Dr Somerville had not had practice in removal of placentas, and if he encountered bleeding after the delivery of a patient he advised him rapidly to plunge his hand in and to go up along the cord until he reached the placenta, and then work it out. He hoped he would get practice in this, and would urge him to have no fear but to go ahead and remove the placenta.

He said he was glad the President had mentioned that in cases of prolonged labour and difficult obstetric deliveries the placenta should not be left *in situ*. He cordially agreed, and if he had such a case from outside, he had no hesitation at all in extracting the placenta immediately after the delivery of the child. In the past he had had to buy his experience with one or two lives.

## NOTES

A QUARTERLY meeting was held on Tuesday, 4th May, the President, Dr W. D. D. Small, C.B.E., in the Chair. Drs Hugh Royal College of Physicians of Edinburgh Adair Raeburn (North Berwick), Graham Malcolm Wilson (Edinburgh) and David Noble Dobbie (Bromley, Kent) were introduced and took their seats as Fellows of the College. Drs Ernest Hume Duff (Selkirk) and Edward Keith Morris (Edinburgh) were elected Fellows of the College. Drs Ralph Campbell Lindsay Batchelor (Edinburgh), Christopher William Clayson (Lochmaben, Dumfries), John Frederick Galpine (Coventry), Robert John McGill (New Milton, Hants), John Ernest Awelrydd David (Bulawayo, S. Rhodesia), Yu Hans Tang (Hong-Kong), Victor Solomon (Johannesburg), George William Senter (Edinburgh), Wyville Smyth Thomson, Jr. (Leicester), Montague Russell Clarke (Cape Town), Clifford Glynn Williams (Durban), Kenneth John Dunlop (Edinburgh), Theodore Barker Binns (Middlesbrough), Allan Vivian Bird (Johannesburg), Robert John Giffen Sinclair (Edinburgh), John Oldroyd Forfar (Dundee), Morris Medalie (Johannesburg), Douglas Kirkwood Stevenson (York), James Richard Fountain (West Hartlepool), Ian Duncan Burton Bottomley (Wallasey, Cheshire), Don Hilson (London), Kemble Greenwood (R.A.M.C.), Bibhuti Bhushan Manna (Bengal, India), Frank Lane Ritchie (Sydney, N.S.W.), Hyman Shrand (Cape Town) and Beatrice Mary Wilson (Edinburgh) were elected Members of the College.

The Lister Fellowship (value, £100), for original research carried out in the Laboratory of the College, was awarded to Dr T. W. Lees (Edinburgh).

Dr Douglas Kerr was re-elected the Representative of the College in the General Council of Medical Education and Registration for a period of five years.

At a meeting of the Royal College of Surgeons of Edinburgh held on 19th May 1948, Mr Frank E. Jardine, President, in the Chair, the following who passed the requisite examinations were admitted Fellows: Clarence Roderick Scott Davidson, M.D. UNIV. TORONTO 1940; Edward Owen Dawson, M.B., CH.B. UNIV. NEW ZEAL. 1940; Thomas Dean, L.R.C.P. AND S. EDIN. (Triple) 1941; Donald MacLeod Douglas, M.B., CH.B. UNIV. ST ANDREWS 1934, F.R.C.S. ENG.; Anup Kumar Dutt, M.B. UNIV. CALC. 1937; Henry Douglas Fairman, M.B., B.S. UNIV. LOND. 1936; Julius Fine, M.B., CH.B. UNIV. WITWATERSRAND 1938; Leo Benjamin Gottlieb, M.B., CH.B. UNIV. WITWATERSRAND 1934; Karam Singh Grewal, M.B., B.S. UNIV. PUNJAB 1933; Eric Gordon Hardy, M.B., CH.B. UNIV. ABERDEEN 1940; Gordon Daniel Jack, M.B., CH.B. UNIV. EDIN. 1942; Zubaida Abdul Karim, M.B., B.S. UNIV. PUNJAB 1942; Stephen Kavanagh, L.R.C.P. AND S. IRELAND 1937; Harsharnsingh Gurmukhsing Khalsa, M.B., B.S. UNIV. BOMB. 1942; Ian Skinner Kirkland, M.B., CH.B. UNIV. EDIN. 1942; John Maynard Large, M.B., CH.B. UNIV. EDIN. 1942; Anthony James Leonsins, M.B., CH.B. UNIV. WITWATERSRAND 1942; David Gerald Lloyd-Davies, M.R.C.S. ENG., L.R.C.P. LOND. 1940; Ernst Jakobus Marais, M.B., CH.B. UNIV. CAPE TOWN 1940; John McElroy Megaw, M.B., B.CH., B.A.O. QUEEN'S UNIV. BELFAST

1938; Narotamdas Vithaldas Mody, M.B., B.S. UNIV. BOMB. 1938; Owen David Morris, M.R.C.S. ENG., L.R.C.P. LOND. 1939; Robert Aloysius McCluskie, M.B., CH.B. UNIV. GLASG. 1944; Andrew Bruce MacLean, M.B., CH.B. UNIV. GLASG. 1942; John Archibald Orr, L.R.C.P. AND S. EDIN. (Triple) 1944; Kyee Paw, M.B., B.S. UNIV. RANGOON 1942; Hugh Norton Perkins, M.B., B.S. UNIV. LOND. 1935; William Rowland Phillipps, M.B., CH.B. UNIV. NEW ZEAL. 1933; Myre Conrad Pinkerton, M.B., CH.B. UNIV. EDIN. 1935; Ernest Hermann Rainer, L.R.C.P. AND S. EDIN. (Triple) 1941; Peter Michael Roemmele, M.B., CH.B. UNIV. EDIN. 1943; Amulya Kumar Saha, M.B. UNIV. CALC. 1938; Antoine Ibrahim Sahyoun, M.D. AMERICAN UNIV. BEIRUT 1945, M.R.C.S. ENG., L.R.C.P. LOND. 1947; Mohamed Mohyi El Din Said, M.B., B.CH. UNIV. CAIRO 1936; Surendra Nath Sarma, M.B., UNIV. CALC. 1941; Ochhavilal Jagjivandas Shah, M.B., B.S. UNIV. BOMB. 1939, M.D. 1941; William David Sharpe, M.D. UNIV. ONTARIO 1939; Bernard James Shaw, M.R.C.S. ENG., L.R.C.P. LOND. 1935; Colin James Cumming Smith, M.B., CH.B. UNIV. EDIN. 1941; Purshottam Bhagwant Sulakhe, M.B., B.S. UNIV. BOMB. 1941; Ronald Vaughan-Jones, M.B., CH.B. UNIV. BIRM. 1936; Osman Wahby, M.B., CH.B. UNIV. CAIRO 1940; Peter Wilson, M.R.C.S. ENG., L.R.C.P. LOND. 1938; Laurence Ewart Wood, M.B., CH.B. UNIV. LEEDS 1944.

## NEW BOOKS

*Suicide and the Meaning of Life.* By MARGARETHE VON ANDICS. Pp. xv+219. London: William Hodge & Co. Ltd. 1947. Price 8s. 6d. net.

This small book is a study of the various factors leading to an attempt at suicide in 100 cases studied at Pötzl's Clinic in Vienna. It is a reasonably comprehensive survey of the objective factors which are present, but it makes no attempt to understand and appreciate the emotional drives which are responsible for the suicidal act. It gives the main facts in relation to suicide, but it does not add anything new to what has been already written. The importance, however, of loneliness and the lack of opportunity to discuss one's problems are rightly given an important place. The book is of general interest but it is of no particular importance to the psychiatric specialist.

*1946 Year Book of Industrial and Orthopaedic Surgery.* Edited by C. T. PAINTER. Pp. 431. Chicago. 1947. Price \$3.75.

The *Year Book of Industrial and Orthopaedic Surgery* could almost be called a small manual of modern orthopaedic surgery. It provides a host of useful information, gives a valuable review of the orthopaedic literature for 1946 and discusses and clarifies many controversial subjects. It is exceedingly well produced, well illustrated and well compiled and can be thoroughly recommended to anyone interested in orthopaedic surgery.

*Miracle Drug: The Inner History of Penicillin.* By DAVID MASTERS. Pp. 191, with 23 illustrations. London: Eyre & Spottiswoode. 1947. Price 10s. 6d. net.

This is an authentic but very personal and dramatised description of the researches and other work which led to the present use of penicillin on such a large scale.

Probably only a small percentage of those reading and enjoying it will realise how genuinely distasteful popular publicity is to laboratory workers and the medical profession in general.

It is illustrated with some very fine photographs.



*Clinical Methods of Neuro-ophthalmological Examination.* By ALFRED KESTENBAUM, M.D. Pp. x+384, with 65 illustrations and 20 tables. London: William Heinemann (Medical Books) Ltd. 1947. Price 25s. net.

The result of twenty-five years' clinical work, this book is based on lectures delivered by the author to neurologists and ophthalmologists and presents the methods of neuro-ophthalmological examination which have greatly increased in recent years. A proper understanding of interference in the visual apparatus constitutes a fundamental feature of neurological diagnosis, yet it is seldom that this aspect of investigation is given its deserved emphasis. In this sense the present volume is a welcome corrective, since the author's experience enables him to present a balanced objective to much that is often obscure in the accurate elucidation of these numerous cases which come equally into the province of the oculist and the physician.

Dr Kestenbaum describes most clearly and concisely the many aspects of clinical defects in the visual mechanism with proof of the bearing that each has in the diagnosis, which is sometimes easy but more often obscure and tricky in elucidation. The description and explanation is often fascinating, and always comprehensible to those who have grasped the essential principles on which neurology is placed. That is to say that the more the reader understands nervous disease the more he will value the teaching contained in these pages.

At the end of the book are to be found three valuable features which are too seldom given in monographs. These are the glossary, the bibliography and author's index, and the subject index itself. Altogether this is a most successful work which is certain to secure a place on the library shelves of every student of nervous disease.

*Nutritional Disorders of the Nervous System.* By JOHN D. SPILLANE, B.Sc., M.D., M.R.C.P. Pp. xv+280, with 103 illustrations. Edinburgh: E. & S. Livingstone Ltd. 1947. Price 20s. net.

This important monograph is sponsored very enthusiastically by Dr George Riddoch. After explaining in his foreword in carefully chosen words the unusually advantageous circumstances available to Dr Spillane for such a study, he concludes by saying, "It is, in fact, an interesting, balanced, and critical account of a fascinating subject."

Much that has for long been difficult to understand is illuminated by the information now given. Many angles are dealt with, for the most part critically, but naturally in many instances inconclusively, which is understandable in a subject still *sub judice*. Yet the total contribution made to a hitherto little known branch of neurology is considerable, and is certain to be a definite step forward to which later contributors will be indebted.

The author deserves great credit for bringing together all his valuable clinical material, ranging from the more obvious to the much more complicated. It is pleasing too to see a number of the present theories, only based on wishful thinking, completely disproved, a feature that authors of text-books on physiology would be well to observe.

This is an excellent monograph, generously illustrated, making a milestone of distinction in a subject that is likely to be a thorny one in spite of exceptionally rapid progress.

*A Synopsis of Orthopaedic Surgery.* By DAVID LE VAY, M.S. (LOND.), F.R.C.S. (ENG.). Pp. viii+242, with 55 illustrations. London: H. K. Lewis & Co. Ltd. 1947. Price 15s. net.

This book, as the author states in the preface, is a concise factual survey of orthopaedic surgery. The material set forth follows closely in substance that of many of the larger works on the subject in general use at present, and as such should prove useful reading for those about to sit examinations in general surgery where orthopaedics enters as a minor part. The choice of subject for some of the illustrations, which are exclusively of the line drawing variety, is in several cases unfortunate, and they provide a poor substitute for photographic representations.

## NEW EDITIONS

*Poisons, their Isolation and Identification.* By FRANK BAMFORD, B.Sc. Second Edition, revised by C. P. STEWART, M.Sc., Ph.D. Pp. viii+304. London: J. & A. Churchill Ltd. 1947. Price 21s. net.

The present edition of this book includes new qualitative and quantitative methods in the identification of poisons, which have been found reliable by laboratory procedures. It is intended as a laboratory manual for all who have to deal with cases of poisoning. Practical methods are employed throughout the book, but enough theoretical material is included to make this a very useful manual for all interested in clinical pathology, biochemistry or forensic medicine.

*Blood Pressure and its Disorders including Angina Pectoris.* By JOHN PLESCH, M.D. Budapest, M.D. Germany, L.R.C.P. AND S. EDIN. AND GLAS. Second Edition. Pp. xiv+307. London: Baillière, Tindal & Cox. 1947. Price 21s. net.

The author discusses the physiological basis of blood pressure and explains the mechanism of hypertension on such a basis. Types of hypertension are described and illustrated by case records. The clinical features and complications of hypertension, including angina pectoris, are discussed at length. The author restricts the scope of this second edition to his own personal observations and research work. The book presents the whole aspect of hypertension, its complications and treatment in a simple, clear and concise manner.

*Heparin in the Treatment of Thrombosis.* By J. E. JORPES, M.D. Second Edition. Pp. 260, with 21 figures. London: Oxford University Press. 1947. Price 18s. net.

Heparin, the physiological anti-coagulant, is as specific in thrombosis as is insulin in diabetes and it is now possible to influence thrombosis to a degree undreamt of a few years ago. Dr Jorpes has produced a complete monograph on the subject, bringing together and critically examining all available information on heparin and its uses. In addition there is a short chapter on dicumarol and its applications.

This important contribution to medical literature will be of interest to physicians and surgeons alike.

*The Treatment of Diabetes Mellitus.* By E. P. JOSLIN, H. F. ROOT, P. WHITE, A. MARBLE, and C. C. BAILEY. Eighth Edition. Pp. 861. London: Henry Kimpton. 1947. Price 50s. net.

No other book on diabetes approaches the completeness of Dr Joslin's monograph on the subject, but as knowledge increases it becomes too vast for one individual to handle, so Dr Joslin has felt compelled to delegate some of the work to some of his experienced colleagues who now become responsible for various aspects of the subject. Extensive revision of the text has thus been possible and the value of the book has been enhanced by the collaboration of this team of experts.

*American Illustrated Medical Dictionary.* By W. A. N. DORLAND, A.M., M.D., F.A.C.S. Twenty-first Edition. Pp. 1660, with 880 illustrations and 226 portraits. London: W. B. Saunders Company. 1947. Price 42s. indexed and 40s. plain.

Originally published in 1900 this dictionary has long maintained a premier position and each successive edition has been thoroughly overhauled. Many new words have been introduced as the result of recent advances and war-time activities.

The words listed are taken from medicine, surgery, pharmacy, chemistry, nursing, dentistry, veterinary science and biology, and in addition there are a large number of thumbnail biographies. Numerous illustrations are introduced to explain the text, and there are many useful tables.

This encyclopædic work will continue to serve an invaluable function.

*A Textbook of Dietetics.* By L. S. P. DAVIDSON, B.A., M.D., F.R.C.P. and I. A. ANDERSON, M.B.E., B.Sc., F.R.C.P. Second Edition. Pp. xix+517. London: Hamish Hamilton. 1947. Price 21s.

The subject of dietetics has grown considerably since the appearance of the first edition and this has involved a considerable increase in the size of the present volume.

The book gives a detailed account of the physiology of nutrition and the composition of food; and individual diseases amenable to dietary therapy are discussed in detail. A specially valuable feature is the amount of space devoted to diet sheets, recipes and tables which should prove of the greatest assistance to those interested in this field.

The book is a thoroughly practical contribution and can be recommended both to the undergraduate and the practitioner of medicine.

*Psychopathology.* By J. ERNEST NICOLL. Fourth Edition. Pp. vii+268. London: Baillière, Tindal & Cox. Price 15s. net.

The fact that this book has now reached a fourth edition is the best indication of its success and of its appeal to a wide public. It presents the views of the acknowledged leaders in the psychopathological field. It does this fairly and yet succinctly enough to be a satisfactory guide both for further study and for the examinations for higher medical degrees. It may be suggested, however, that the chapters on Endocrine Theories, Biochemical Findings, and Physiological and Anatomical contributions might be omitted in any future edition as they have been gathered together in a rather uncritical manner and take away from the value of the book.

## BOOKS RECEIVED

- LUND, C. G., NIELSEN, E. PEULICKE, and PEDERSEN-BJERGAARD, K. The Preparation of Solutions Isoosmotic with Blood, Tears, and Tissue. (Messrs William Heinemann (Medical Books) Ltd., London) 15s. net.
- MARTIN, C. R. A. Practical Food Inspection. Vol. II—Fish, Poultry, and Other Foods. Third Edition (H. K. Lewis & Co. Ltd., London) 18s. net.
- MCDONAGH, J. E. R., F.R.C.S. The Nature of Disease Institute. First Annual Report (William Heinemann (Medical Books) Ltd., London) 21s. net.
- NEATHY, EDWIN A., M.D.LOND., and STONHAM, THOMAS GEORGE, M.D.LOND. A Manual of Homœo-Therapeutics. Third Edition. (Staples Press Ltd., London) 32s. net.
- NEUSTATTER, W. LINDESAY, M.D., B.Sc., M.R.C.P. Modern Psychiatry in Practice. Second Edition (J. & A. Churchill Ltd., London) 12s. 6d.
- PARSONS, Sir JOHN HERBERT, C.B.E., D.Sc., F.R.C.S., F.R.S., and DUKE-ELDER, Sir STEWART, K.C.V.O., M.A., D.Sc., PH.D., M.D., F.R.C.S., HON. D.Sc. Diseases of the Eye. Eleventh Edition (J. & A. Churchill Ltd., London) 30s.
- POTTENGER, FRANCIS MARION, A.M., M.D., LL.D., F.A.C.P. Tuberculosis. (Kerry Kimpton, London) 60s. net.
- Edited by PULAY, E., M.D., and LANSEL, P., M.D. Constitutional Medicine, Endocrinology, and Allergy. Vols. II, III, and IV. (Frederick Muller Ltd., London) 10s. 6d. net each volume.
- ROMANIS, W. H. C., M.A., M.B., M.CH.CANTAB., F.R.C.S.(ENG.), F.R.S.(EDIN.), and MITCHINER, PHILIP H., C.B., C.B.E., T.D., M.D., M.S.(LOND.), F.R.C.S.(ENG.), D.CH.(DURHAM). The Science and Practice of Surgery. Eighth Edition. Vol. I: General Surgery; Vol. II: Regional Surgery. (J. & A. Churchill Ltd., London) 25s. each volume
- Issued by The Medical Officers' of Schools' Association. Handbook of Communicable Diseases for the Use of Medical Officers of Schools. Formerly a Code of Rules. Eleventh Edition (J. & A. Churchill Ltd., London) 5s.
- TRAQUAIR, H. M., M.D., F.R.C.S.ED. Clinical Ophthalmology. For General Practitioners and Students. (Henry Kimpton, London) 25s. net.
- WHITING, MAURICE H., O.B.E., M.A., M.B., B.CH.(CANTAB.), F.R.C.S. Ophthalmic Nursing. Fifth Edition (J. & A. Churchill Ltd., London) 7s. 6d.
- WINTON, F. R., M.D., D.Sc., and BAYLISS, L. E., PH.D. Human Physiology. Third Edition (J. & A. Churchill Ltd., London) 25s.



# Edinburgh Medical Journal

June 1948

## THE NEWBORN: SOME PROBLEMS OF SURVIVAL \*

By RICHARD W. B. ELLIS, M.A., M.D., F.R.C.P.  
Professor of Child Life and Health, University of Edinburgh

THE importance attached to the survival of the newborn infant has varied immeasurably through the centuries, and also between different communities in the same era. Even at the present time it depends to a large extent on sex, race, rank in family, legitimacy, and other factors which render the future of the newborn the sport of chance. Of all members of the community the newborn is least able to control his own destiny. Unlike the aged and outworn, who may be a greater burden on the State, he has no vocal contemporaries who can plead his case and no record of previous service to justify his continued consideration. When he has survived, it has been in virtue of future promise, and as an investment or nest-egg which is expected to pay future dividends.

It would probably be true to say that the newborn has never received more consideration than he does in most civilised countries to-day. But it is worth considering briefly how and why this has come about, how far it is justified, and of how recent growth this cult of baby-worship may be. Has it reached its zenith already, or can we look forward to more and better babies, and, if so, by what means can this object be achieved? These are questions which I cannot attempt to answer, but I should like to present a little of the raw material from which the answers may ultimately emerge. In the first instance, it should be remembered that whilst the neonatal mortality (deaths under one month) has been substantially reduced in this country during the present century, the reduction of newborn deaths has been less dramatic than the decrease of post-natal mortality (deaths from 1 to 12 months). This in itself provides a reason for concentrating attention on the newborn.

*Reproduction and Wastage.*—The process of reproduction provided by nature for every species including man, is one which allows for such a high percentage of wastage that the survival of all possible progeny from every mating is unthinkable. It is true that as the scale is

\* Read at a meeting of the Medico-Chirurgical Society of Edinburgh on 4th February 1948.

ascended, the wastage becomes less. Thus the time taken to reach maturity becomes longer and the period of gestation increased. In man, the reproductive period is further limited by a period of relative sterility in both sexes after secondary sexual characters have appeared—the so-called adolescent sterility (Montague, 1946)—and a period of relative infertility before the menopause in the female or absolute sterility in the male is reached. The reproductive cycle is itself so restricted that conception is only likely to occur during a comparatively small number of days each month. But even with these limitations,

NEONATAL, POSTNATAL, AND INFANT MORTALITY RATES PER  
1000 LIVE BIRTHS.  
QUINQUENNIAL AVERAGES : EDINBURGH

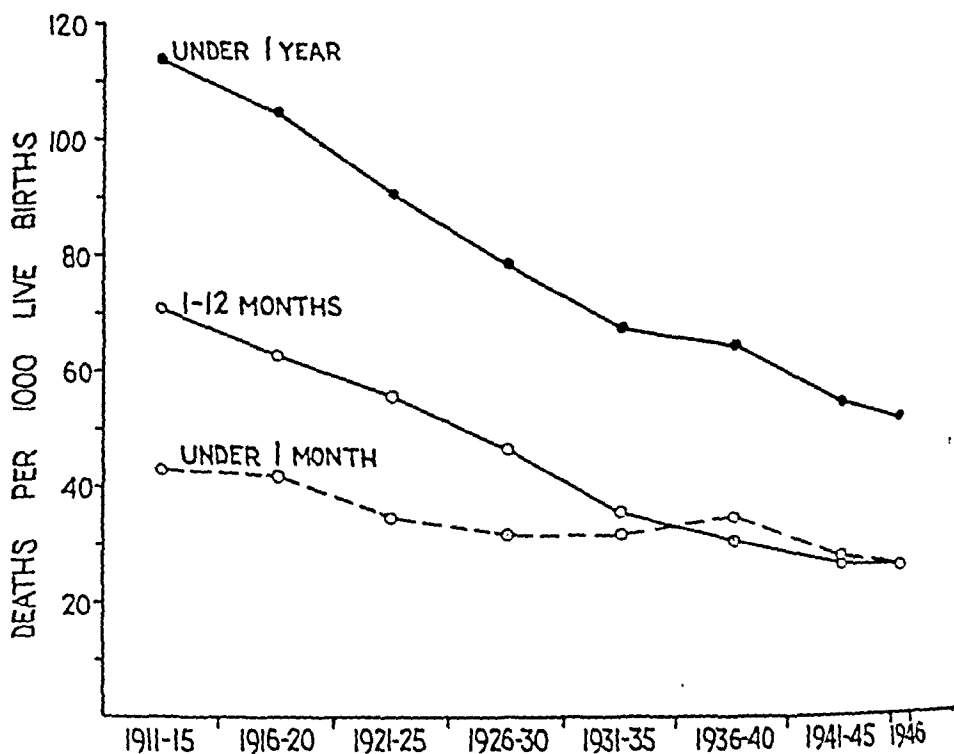


FIG. 1.—Edinburgh. Reduction of the total infant mortality rate is shown to be due principally to reduction in death-rate from one to twelve months. Ratio of neonatal to post-natal deaths for quinquennium 1911-14 was 43:71. In 1946, the ratio was 26:26.

many human couples would be capable of engendering between twenty and thirty foetuses during their reproductive life, and indeed the bearing of fifteen to twenty living infants is not by any means phenomenal. Since popular interest is always aroused by extreme fecundity and multiple births, the literature abounds with examples of variable authenticity. Thus the press has recently carried the story of an English mother of seventeen children who became a great grandmother at the age of fifty-three, whilst Ploss *et al.* (1935a), quote the case of a negress who gave birth to sixteen children in five pregnancies, and examples of sextuplet and septuplet births, some at least of which are

probably authentic. It is significant, however, that the mortality of multiple births and births of great multiparity is high.

*Infanticide*.—Until comparatively recent times, the dangers of over-population of the globe were limited by a naturally high neonatal and infant mortality, famine, epidemic disease, and war. Where these were insufficient, man himself took a hand in increasing the neonatal mortality, and infanticide was a common practice amongst primitive people. Ploss *et al.* (1935), give numerous examples, and it is of interest that in the majority of these cases there was a selective destruction of female infants rather than of male. Thus in Hindustan the destruction of female infants survived until comparatively recently; the pre-Islamite inhabitants of Arabia buried female infants in the sand, the natives of Greenland in the snow. The Hak-Ka tribe in South China immersed them in a domestic utensil, and it is estimated that two-thirds of female infants were so destroyed. Rare examples of selective destruction of males are described in matrilineal societies, *e.g.* Fijians and Banks Island natives, whilst in certain Uganda tribes the firstborn was killed if a son, since otherwise it was believed that the father was doomed.

In New Guinea, on the other hand, newborn infants were killed irrespective of sex if they were deformed or had suffered prolonged or difficult delivery, whilst amongst the Australian aborigines infanticide was widely practised with only partial preference given to survival of the male.

Sex discrimination against the female is of particular interest when it is considered in relation to present-day vital statistics. From these it is clearly obvious that the chances of survival are heavily weighted against the male. This would be easily understandable if it applied only to birth injury (since the male infant is on the average slightly larger than the female) or to other traumatic causes of death, but it runs throughout almost every age period and applies to such various conditions as respiratory infections, intestinal obstruction and prematurity. To take two random examples from near home, the incidence of gastroenteritis amongst newborn in the Simpson Memorial Pavilion was, from a recent analysis made over an eight-year period (Thomson, 1948), 308 cases; of these 181 were males and 127 females, the mortality being 60 males and 42 females. The incidence of hæmorrhagic disease of the newborn in the same hospital over a similar period was 27 males and 17 females. One is reluctantly forced to the conclusion that the male is in fact the weaker vessel, and it is poor consolation to learn that in 1945 amongst Scottish ladies aged ninety-five to a hundred, deaths by violence were nine times as frequent as amongst males.

Thus female infanticide was a rough and ready method of redressing the balance of the sexes at an early stage in life.

*Illegitimacy*.—When we come to consider infanticide in Great Britain in the eighteenth and nineteenth centuries, we find that it was no longer based on sex-discrimination but largely depended on whether

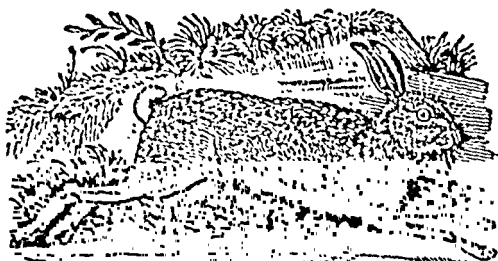
the infant was legitimate or born out of wedlock. This insistence on the infant being a member of a family unit can be paralleled amongst primitive tribes, e.g. in the Solomon Islands where the infants born out of wedlock were destroyed, but appears to have reached its maximum intensity with the economic pressure of the industrial era. The employment of female labour in factories rendered the illegitimate infant a burden which many women were eager to shuffle off, and the absence of any organised care for the unwanted newborn resulted in most of these infants dying of exposure or by other means. Captain Thomas Coram was led to establish the Foundling Hospital in 1739 from his concern at the number of dead infants he saw thrown out on dung hills. But this beginning proved pitifully inadequate to meet the demand, and when a government grant was obtained for the hospital on condition that all infants brought to its doors must be accepted, the mortality within the hospital itself rose to 66 per cent. (Nichols and Wray, 1935), and both government grant and indiscriminate admission had to be abandoned.

During the nineteenth century, infanticide became almost a recognised profession, and "baby farmers" flourished in a society where there was a steady supply of infants for disposal with no questions asked. Owing to the unreliability of registration of both births and infant deaths, the total number of infants who were destroyed or allowed to die from neglect can never be known, but when the Society for the Preservation of Infant Life was founded in 1870 it was estimated that of all infants handed over to baby farmers, between 60 and 90 per cent. died. As late as 1896, the trial of Mrs Dyer proved that infanticide for profit was still being practised on a considerable scale.

During the present century, legislation and a certain reorientation of social conscience has reduced the systematic destruction of illegitimate infants, but there is still a very considerable bias against their survival as compared with that of legitimate infants. Thus in England and Wales in 1939, the neonatal mortality rate (deaths under four weeks) for all infants was 28.3 per 1000 related live births, whereas that for illegitimate infants was 50.7; the corresponding infant mortality rates (deaths under one year) were 44.4 and 90.0 respectively. In Scotland, McKinlay (1948*a*) has shown that in the triennium 1943-45 the infant mortality rate of illegitimate infants shows an excess over the general rate of the order of 60 per cent., the relative disadvantage of illegitimate infants being most obvious in deaths from syphilis, diphtheria, abdominal tuberculosis, debility, overlying, diarrhoea and prematurity. In stillborn infants, the excess mortality in illegitimates is in the order of 20 per cent., indicating that even before birth the scales are weighted against the illegitimate infant.

This excessive stillbirth rate and the still more excessive neonatal and infant mortality rates are, in the last analysis, an index of society's reaction to the unmarried mother and her child. During pregnancy the mother, and after birth the infant, receive less care and are exposed

faster,



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vitamin B <sub>1</sub>	0.45 mg.	vitamin E	8.0 mg.	protein	30%
vitamin B <sub>2</sub>		manganese	4.0 mg.	available carbohydrate	39%
(riboflavine)	0.3 mg.	iron	2.7 mg.	fibre	2%
nicotinic acid	1.7 mg.	copper	0.45 mg.	calorific value	104
vitamin B <sub>6</sub>	0.45 mg.				

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to greater risks than those that form part of a normal family unit. The difference is not solely an economic one, though the support of a wage-earner is undoubtedly of very great importance. Even in the case of an unmarried mother who is economically independent, the difficulties in keeping and rearing her child are such that an alternative is usually preferred. Again, in modern states where official efforts have been made to encourage reproduction without marriage or to render divorce so easy that marriage is largely nominal, the experiments cannot be said to have met with any great measure of success. But

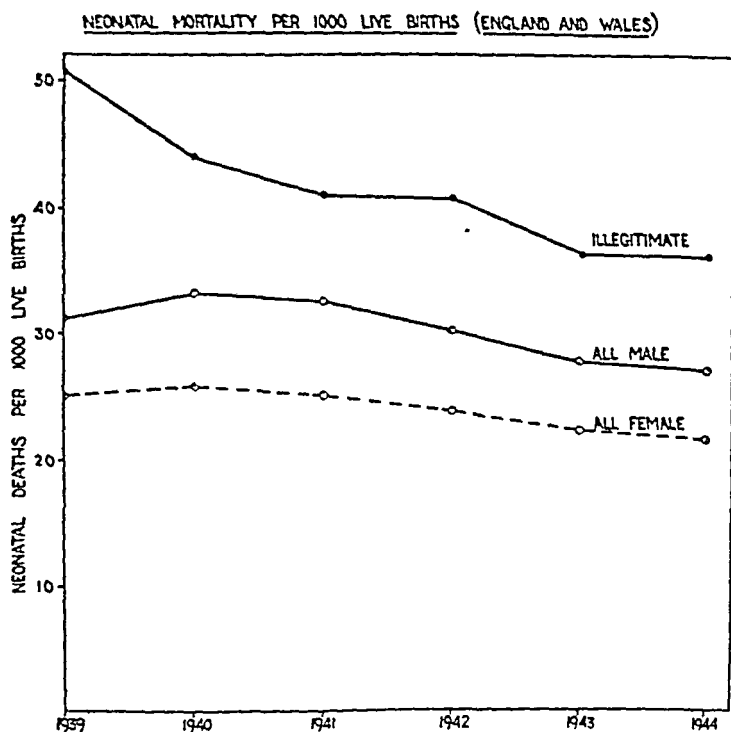


FIG. 2.—Neonatal mortality rates of all male, all female, and illegitimate infants in England and Wales (1939-44). The illegitimate neonatal death-rate is consistently higher than the general neonatal death-rate, and the neonatal death-rate of males higher than that of females.

whilst one must reach the somewhat platitudinous conclusion that marriage is a biologically sound institution, and that the family unit provides the infant with the best prospects of survival, there is clearly much that can still be done to improve the status of the illegitimate child. When it is remembered that in Scotland in 1945, illegitimate births represented 8.57 per cent. of all live-born children (the highest percentage recorded this century), it will be realised that illegitimacy is one of the major problems of the newborn period. Care of these infants can be attempted along one of various ways:—(1) Improved facilities for the unmarried mother to care for her own child, including extended provision of hostel accommodation before and after the birth

of the child, (2) legal adoption, (3) care in foster homes, and (4) care in institutions. Of these four, care of young infants in institutions is probably the least satisfactory, even when such units are small and adequately staffed and equipped. The infant can never receive the same individual attention as in a private home, and "the institution child" is an inevitable product. Unfortunately, some at least of the large voluntary organisations which had previously boarded out infants in foster homes have had to revert to this group system owing to the difficulty of finding suitable foster parents under present circumstances. The good foster home can, of course, have many of the advantages of the family unit, though where infants are boarded out for payment, and the same foster parents take on successive children over many years, the bond between any individual child and its foster parents tends to be loose and readily shaken off. Many of these children pass on to institutions when infancy is passed.

*Certification of Birth.*—In order to prevent the stigma of illegitimacy appearing on the birth certificate (whether the child be adopted or not), a shortened form has recently been introduced in England which omits details of parentage but is sufficient for all ordinary purposes. In order that this protection shall be effective, however, it is highly desirable that the shortened form should be that commonly used for both legitimate and illegitimate infants, and it is interesting to note that although the shortened form is cheaper there is some reluctance to use it for legitimate infants. One practical way in which doctors can help to relieve the disadvantage from which the illegitimate members of the community suffer, is to recommend all parents to use the shortened form of certificate for all ordinary purposes when date of birth only is required.

*Legal Adoption.*—Where circumstances make it impossible for the unmarried mother to keep her child, there is much to recommend legal adoption in early infancy. This must, however, be adequately supervised, for the protection both of the child and the adopting parents. If applications for adoption are carefully scrutinised it will be found that they are sometimes made from such motives as desire to cure a partner of drunkenness or neurosis, and that no real consideration has been given to the welfare of the child. On the other hand, couples may wish to adopt a particular infant with no realisation of its unsuitability. One example of this was recently encountered when no less than five mothers in a ward were so attracted by an illegitimate baby that they more or less seriously said they would like to adopt it. On enquiring the reasons, three said it was "so good," *i.e.* did not cry, two said it was small, and all added that it was "so sweet." The infant was, in fact, a premature mongolian idiot with congenital morbus cordis.

A point that often receives insufficient attention is that the unmarried mother is often faced with the decision as to whether she should keep or give up her infant during the puerperium. Of all times in her life, this is probably the one at which she is least well able to face

making a major decision on her own initiative, and great responsibility lies on whoever urges one course or the other. If the mother has been admitted to a hostel before delivery, she will have had the opportunity of asking advice beforehand, but it cannot be too strongly emphasised that whoever gives it should be a person of real understanding and sympathy, who is ready to go into the individual circumstances in detail, and who does not start with preconceived principles that "all unmarried mothers" should be bullied into doing this or that. Spence (1946) has painted a gloomy picture of a future in which the welfare of children may fall more and more into the hands of spinsters or civil servants who are themselves only children and have little conception of what the family really means. I would urge that every hostel for unmarried mothers should have on the staff at least one carefully chosen woman who has had children of her own, legitimate or otherwise. Indeed, since approximately seven thousand illegitimate children are born in Scotland every year, and fifty-four thousand in England and Wales, it should not be difficult to select from this great number of unmarried mothers a proportion for training as house mothers who would be well fitted for this work, and would approach it with an understanding which is only acquired laboriously, if at all, by the more orthodox social worker.

*Maternal Illness.*—Maternal illness requiring separation from the infant is another problem of the newborn period which in this country is still very inadequately met. The outstanding example is open pulmonary tuberculosis in the mother. Here the newborn infant runs a grave risk of infection if it is in contact with the mother, and the risk is little reduced by weaning the infant if the mother is bottle-feeding it herself. Ideally, the infant should be completely separated from birth until the mother has become sputum-negative. In many European countries, B.C.G. inoculation has been used with the purpose of increasing the infant's immunity during the period of separation. Unfortunately, there is no conclusive evidence as to the effectiveness of antibody formation by this means during early infancy. It is known that the newborn does not readily develop antibodies, and B.C.G. inoculation is usually delayed until the second month of life. The vaccine is given in relatively larger doses than to older children to produce positive tuberculin reactions (which cannot be regarded as any exact measure of immunity). Since the results must be assessed in clinical trials, it is only possible to say at present that the weight of evidence is becoming more favourable to the use of B.C.G. in general, and that medical opinion in Great Britain has probably been unduly influenced against its use by the statistical criticism of the earlier claims presented.

*Stillbirth and Neonatal Mortality by Social Class.*—It has been increasingly recognised that the stillbirth, neonatal, and post-natal mortality rates are lowest amongst the more well-to-do classes, and tend to increase with "poverty." Classification of infant and foetal

receiving supplements containing minerals and Vitamins A and D, B complex, and C. The effect on foetal death, however, were not striking, and when the stillbirths and deaths under eight days are added together the figures for the controls and treated groups are almost identical.

Balfour (1944) claimed a significant reduction in the incidence of stillbirth and neonatal mortality in the infants of mothers receiving a supplement of Vitamin B complex, but in neither of these two experiments were the constituents of the basic diet at all accurately assessed.

Although based on a much smaller number of cases (a total of 216 mothers), a study made by Burke *et al.* (1946) in Boston is considerably more informative with regard to the relation of maternal diet to the status of the infant at birth. These workers approached the problem of prenatal nutrition from a somewhat different angle, the diets of mothers from the first antenatal visit to time of delivery being assessed from a detailed dietetic history as excellent, good, fair, poor and very poor. The infants born were assessed by the obstetrician at time of delivery and subsequently by a pædiatrician during the neonatal period; the gradings given were superior, good, fair and poorest. When these two ratings were correlated, it was found that of the infants judged superior, 56 per cent. of the mothers had been on an excellent or good diet, 35 per cent. fair, and 9 per cent. poor to very poor. Of the poorest infants, 3 per cent. of mothers had been on a good or excellent diet, 18 per cent. on a fair diet, and 79 per cent. on poor to very poor diets.

Again, when the mothers were divided into those who had been on an excellent or good diet, a fair diet, or poor to very poor diet, the infants in the first group were found to be 42 per cent. superior, 52 per cent. good, 3 per cent. poor and 3 per cent. poorest. Of the mothers on a poor to very poor diet, 3 per cent. of the infants were superior, 5 per cent. good, 25 per cent. fair, and 67 per cent. poorest. In addition, all the infants who were stillborn, all who were premature, and all except one dying within a few days of birth, were born to mothers whose diet during pregnancy were very inadequate.

The effects of extreme deprivation during pregnancy have been studied in Holland by Smith (1947), where a sharply limited period of severe malnutrition occurred from September 1944 to May 1945. Diets of pregnant women were particularly deficient in calories, protein, calcium, Vitamin A, niacin and riboflavin. Smith found evidence that during the last half or trimester of pregnancy this had interfered with the prenatal growth of infants as shown by foetal weight and length. Menstruation ceased in approximately 50 per cent. of urban women and became irregular in 50 per cent. of the others. Data as to abortion and miscarriage were not statistically reliable. There was a slight but significant increase in premature birth, but figures relating to neonatal mortality (which were dubiously valid) did not demonstrate an increase, and those in relation to congenital abnormalities were inconclusive, (being invalidated by amenorrhœa and low conception

rate). Lactation as judged by ability to feed an infant, was not significantly influenced.

There is as yet no conclusive evidence that dietetic deficiency in early pregnancy is liable to produce congenital deformities in human infants, though there is considerable experimental evidence (Warkany, 1947), that deformities of the eyes, ears, and palate may be determined by controlled vitamin deficiencies in pregnant sows and rats.

*Causes of Stillbirth and Neonatal Death.*—Before considering these in detail, it should be emphasised that many of the statistical studies published have been based on the Registrar General's Reports. These in turn are entirely dependent on correct certification of the cause of death. In no group of cases is unaided clinical assessment of cause of death likely to be more at fault than in dealing with the newborn, and both intracranial hæmorrhage and infection are particularly liable to be overlooked. In fact, Spence and Miller (1939), in a study of infantile deaths in Newcastle reached the conclusion that in a third of the total cases certification of death had been inaccurate. The fact that approximately 10 per cent. of neonatal deaths in the Registrar General's reports are described as "congenital debility" (as distinct from prematurity) is itself an indication that in a substantial proportion of deaths the cause remains virtually undiagnosed. It may be urged that analysis of post-mortems on infants dying in maternity hospitals are not representative, since hospital practice will tend to be overweighted with abnormal deliveries. But until post-mortem examination of stillbirths and neonatal deaths occurring in domiciliary practice is much more general than it is at present, hospital records are probably more representative than analyses based on national certification.

Prematurity may be regarded as a contributory cause of death in more than 50 per cent. of infants dying within the newborn period, and its role in stillbirth is almost equally important. Thus in Drillien's (1947) analysis of neonatal deaths occurring in the Simpson Memorial Maternity Pavilion in 1943-5, 142 were premature and 62 full term; similarly in McGregor's (1946) analysis of 618 post-mortems on newborn infants dying in the same hospital, 436 were premature, though prematurity was regarded as the primary cause of death in only 9 per cent. of the total series. In 453 post-mortems on stillborn infants (McGregor 1946), 235 were premature and in 51 (21·7 per cent.) of the premature group no other cause of death was found. (Drillien's figures show a similar though slightly lower ratio of premature to mature or post-mature stillbirths viz., 177; 195). Since the prevention of prematurity is partly an obstetric and partly a social problem, I will only here mention the importance of diet during the antenatal period; the general health, age, and parity of the mother; the early recognition and treatment of maternal infection, *e.g.* syphilis; the prevention and treatment of toxæmia; and the general principles of antenatal care. There remain, however, a considerable proportion of premature births of which the cause is unknown. Although much

can be done post-natally for the successful rearing of premature infants, it is at best a laborious and often discouraging substitute for prevention. With this qualification, however, it should be said that remarkably good results have been obtained by Dr F. J. W. Miller of Newcastle in the domiciliary treatment of prematures, where a trained nursing service has been organised; except for the smaller prematures, the results in most unpromising surroundings bore comparison with those obtained under optimum hospital conditions.

Apart from the contributory role played by prematurity, the causes of neonatal death in McGregor's series were, in order of importance, infections (30·7 per cent.), intracranial hæmorrhage (27·6 per cent.), asphyxia (13·1 per cent.), and developmental defects (10·5 per cent.). In the stillbirth series, the most important causes were asphyxia (37·2 per cent.), intracranial hæmorrhage (24·1 per cent.), and developmental defects (20·2 per cent.). Here infections accounted for only 3·2 per cent. of all stillbirths. Where neonatal deaths after the third day were analysed separately, it was found that infection accounted for 65·5 per cent.

*Neonatal infection* must therefore be regarded as of outstanding importance, particularly after the first forty-eight hours of the neonatal period. This is understandable, since the newborn infant has only a limited congenital immunity to certain infections, to which the mother is herself immune, and is otherwise poorly able to produce antibodies. Inhalation of liquor amnii or meconium during birth, or subsequently of vomitus in the case of feeble infants, will increase the likelihood of pulmonary infection, whilst prematurity is again a predisposing factor.

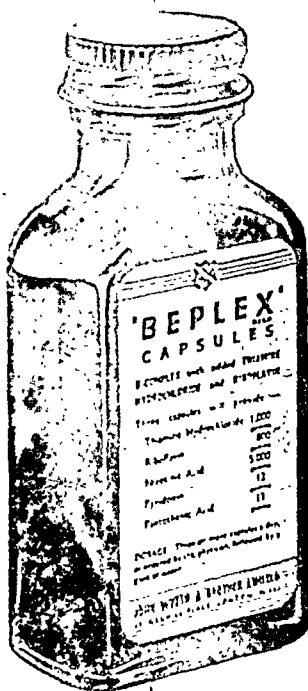
It has been pointed out (Ludlam, 1947) that the foetus is normally sterile until the rupture of the membranes occurs, at which time it comes in contact with the vaginal organisms. Apart from the risk of gonococcal infection of the eyes, against which prophylactic measures are normally taken as routine, the infant may at this time inhale contaminated liquor or become infected with thrush. This latter infection is often troublesome and may result in feeding difficulties during the newborn period, but is seldom fatal unless it extends to the oesophagus or stomach.

Of fatal infections during the newborn period, pneumonia (occurring either alone or in association with other conditions) is the most important. McGregor (1947) recognises four types characteristic of this age, viz. pneumonia occurring in the first week and affecting lungs which are atelectatic or containing inhaled liquor, septic aspiration pneumonia due to inhaled milk or vomitus, staphylococcal pneumonia, becoming suppurative, and bronchopneumonia due to air-borne infection with a variety of organisms including hæmolytic streptococci, pneumococci or *H. influenza*. The clinical diagnosis of pneumonia in the newborn is particularly baffling. Not only are physical signs frequently indefinite, but there is often little or no temperature response and no characteristic tachypnoea. Cyanosis or pallor, lethargy, refusal

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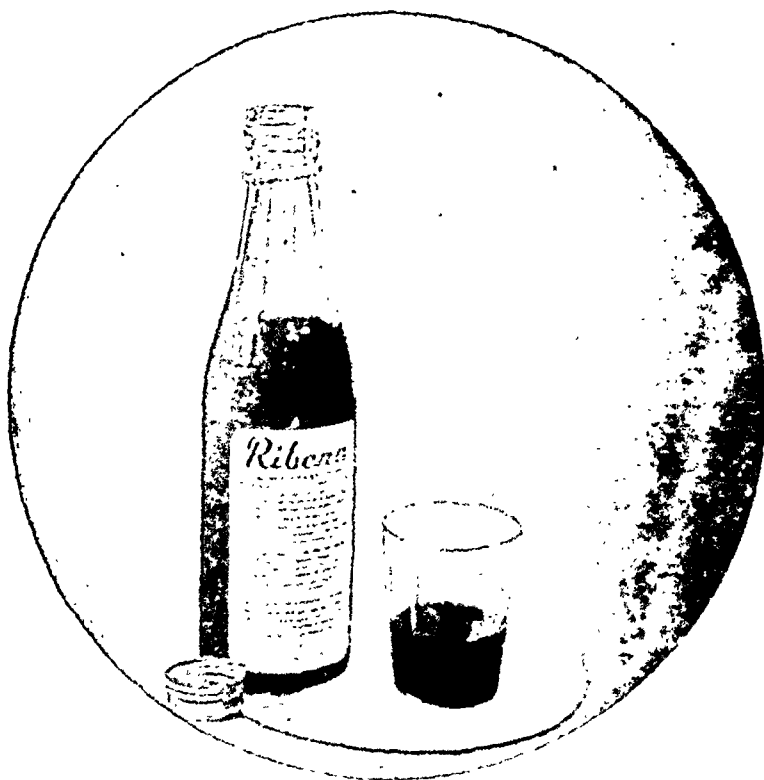
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to suck, feeble cry, and loss of weight may be the only presenting symptoms. X-ray is often inconclusive. Pneumonia should be suspected whenever there has been failure to expand the lungs after a difficult delivery, or inhalation of liquor, and when the newborn fails to thrive. Prophylactic use of oral penicillin (10,000 units three hourly) appears justified in such cases, though in the absence of clear physical or radiological signs it is difficult to assess its effectiveness.

Epidemic diarrhoea of the newborn has recently received considerable attention, and outbreaks have been described in Great Britain, Europe, and America. There is experimental evidence that the condition is, or at least may be, due to virus infection. The mortality has varied in different epidemics but has usually been high. Both breast and artificially fed infants are liable to be infected. In one epidemic personally observed in a maternity unit in London, the case incidence was extremely high (breast-fed infants showing no immunity) but the mortality minimal. In this instance, a number of the mothers were also affected with mild diarrhoea, and a few showed temperatures of  $99^{\circ}$  to  $100^{\circ}$ . A detailed bacteriological investigation of both mothers and infants revealed no causative organism. Onset of the disease in infants occurred after the third day and was sudden; the passage of an explosive, watery stool was usually the first evidence of infection. In a minority of cases, diarrhoea was preceded by refusal of a feed or lethargy, but these symptoms were seldom noted more than a few hours before onset of diarrhoea, making effective isolation almost impossible. The majority of infants showed mucus in the stools at some time, but no blood. The striking feature of the outbreak was the high infectivity, and spread occurred throughout the unit in spite of all efforts to prevent cross-infection. When the unit was closed and reopened, cases again occurred, due probably to the incidence of diarrhoea amongst mothers in the district served by the hospital. Treatment with sulphaguanidine appeared ineffective.

Although large scale epidemics are fortunately rare, neonatal diarrhoea is a constant danger when large numbers of infants are kept together in newborn nurseries.

Other infections liable to affect the newborn are staphylococcal skin sepsis, umbilical sepsis, and septicaemia. Pyelitis in the newborn is commonly associated with congenital abnormalities of the genito-urinary tract, and may be manifested clinically by anaemia and failure to gain weight. Whilst the majority of cases of skin sepsis remain mild and limited to a few small pustules, the danger of extension, and also spread from infant to infant, is much greater in the newborn than in older patients. Unless the bathing of newborn infants can be carried out with rigid precautions, it is better omitted in a newborn nursery.

*Intracranial Haemorrhage.*—It has been claimed that minimal degrees of haemorrhage, giving rise to no clinical symptoms and to no after-effects, are likely to occur in a substantial proportion of newborn infants, particularly prematures. But since these claims are based

largely on the finding of red cells or xanthochromic fluid in otherwise normal infants on whom routine lumbar puncture was done during the newborn period, this interpretation of the findings must be viewed with considerable reserve (Ehrenfest, 1931). There is also considerable difference of opinion as to whether asphyxia *per se* is liable to produce intracranial hæmorrhage (as distinct from small petechiæ), though the two conditions may be associated. Tearing of small or larger vessels sufficient to produce clinical symptoms or death is either the result of abnormal birth trauma or of immaturity of an infant whose tissues are unable to withstand a degree of trauma which would be harmless to an infant at term. In McGregor's series (1946), intracranial hæmorrhage was regarded as the cause of death in 32·3 per cent. of the premature and in 17 per cent. of the mature neonatal deaths. It was present in 24·1 per cent. of the stillbirths. The hæmorrhage may be subdural (from tearing of the vessels draining into the longitudinal sinus), subarachnoid, intraventricular, intracerebral, or occur in a combination of sites. Large tears of the falx (such as are liable to occur when there is great distortion of the foetal head) or of the tentorium or great vein of Galen, are likely to prove rapidly fatal or result in stillbirth. Such lesions are notoriously liable to occur in breech deliveries.

Major hæmorrhage is usually shown by lethargy, twitching, failure to suck, irregularity of respiration and possibly by bulging of the anterior fontanelle and separation of the sutures. In some cases the clinical picture will be similar to that of infection, *e.g.* pneumonia. Lumbar puncture is likely to clarify the diagnosis in the case of subtentorial hæmorrhage, though blood-staining of the fluid more frequently occurs in newborns as a direct result of lumbar puncture than in older infants. In subdural hæmorrhage subdural tap through one or both sagittal sutures, laterally to the longitudinal sinus, may be necessary. In some cases of subdural hæmorrhage it is possible to relieve pressure by aspiration or later by operative removal of the clot, but the prognosis is always poor when the hæmorrhage is extensive. The administration of Vitamin K to the mother before delivery and to the infant after birth is indicated as a routine when there is any danger of intracranial hæmorrhage occurring, as in premature or difficult delivery. True hæmorrhagic disease of the newborn in which the prothrombin level of the blood is likely to be abnormally low, and in which hæmorrhages may occur in any site, particularly the gastrointestinal tract, sometimes gives rise to petechial or gross cerebral hæmorrhage; here the hæmorrhages are most likely to occur on the second to fourth day of life.

Apart from major hæmorrhage, however, it is found that many infants suffer some degree of shock during the birth process. In a series of 173 full-term deliveries in the Simpson Memorial Maternity Pavilion (127 spontaneous, 46 forceps), the infants were classified on the basis of cry, colour, reflexes, muscle tone, respiration, etc. into those who showed any abnormality however slight and those who were

regarded as completely normal. It was found that of the forceps deliveries, 22 per cent. of the infants were classified as "abnormal," whilst of those delivered spontaneously 6 per cent. were classified as "abnormal." As would be expected, the analysis also indicated that high forceps delivery was more likely to result in evidence of shock than when low forceps were applied, (Balf 1948).

Although the general standard of midwifery has greatly improved in Great Britain during the present century, and some of the birth-deaths must be regarded as inevitable, there is little doubt that neonatal mortality and birth injury can still further be reduced by a yet higher standard of obstetric care. Indeed, the figures for both America and Great Britain suggest that the mortality from birth injury is actually rising (Evans and Russell, 1947), though here allowance must be made for more accurate certification.

Asphyxia, which is an important cause of stillbirth and neonatal death, is also largely an obstetric problem, but here the prompt use of oxygen after birth and the prevention of infection may save a proportion of infants who would otherwise succumb.

*Congenital abnormalities* represent a cause of infant death, and disability in those that survive, that until recently has offered little cause for optimism. Such abnormalities account for approximately 10 per cent. of stillbirths and 20 per cent. of neonatal deaths, there being a tendency for neonatal deaths from this cause to rise when the stillbirth rate is reduced, *i.e.* a proportion of congenitally deformed infants being liveborn and subsequently dying, who would previously have died during pregnancy.

Recently, however, the recognition by Gregg (1941), Swan (1944), and others that maternal infection, *e.g.*, rubella during pregnancy may cause congenital abnormality if it occurs at the period of organogenesis, opens a new field of approach, whilst the experimental work of Warkany (1947) on the effects of nutritional deprivation during early pregnancy suggests another. Even the modes of the inheritance of those abnormalities which are genetically determined may in some instances be sufficiently understood for it to be possible to give advice on the likelihood of abnormality occurring as the result of a particular mating. Haemolytic disease of the newborn, in so far as its occurrence depends on the rhesus constitution of the parents, is a case in point, whilst the understanding of its cause has led to a significant lowering of case-mortality.

It has been said that a good egg in a bad environment may develop in much the same manner as a bad egg in a good environment, and though we are not yet sufficiently skilled eggglers to eliminate all the bad eggs we can at least hope to see eventually the great majority of good eggs going into good baskets.

In conclusion, I would like to return to the questions originally asked. Can we expect more babies? The downward trend of the birth-rate in Great Britain has recently shown a significant improve-

ment, but it is too early to say whether this is a purely temporary reaction to war conditions. The position is complicated by the fact that contraception has to a large extent replaced infanticide as a means of limiting the population, and in spite of the good work carried out by numerous clinics is still to a large extent "control without control." Delay of marriage and reproduction until relatively late in the reproductive age period are factors which adversely affect the birth-rate, and which affect different social classes somewhat unevenly. I do not propose to discuss the vexed question of artificial insemination, though the problem of the infertile marriage is a very considerable one, which can only partially be solved by the systematic study of sterility. Better organisation of the system of adoption offers one method by which childless couples can rear healthy children, and help to reduce the high mortality of illegitimate infants.

As to the production of better babies, there seems no question that this can be done. Not only the nutrition of the mother during pregnancy but her physique before she becomes pregnant are of first importance, so that any improvement in social conditions is only likely to bear full fruit in one or more generations.

Whether or not the care of the newborn has reached a maximum, will depend in the last analysis on economic and international factors which we cannot foresee. But I would emphatically urge that there is much more yet that can usefully be done, both in reducing the present wastage of foetal life and in giving those infants that survive the optimum chance of future health. It has recently been estimated that the stillbirth rate in Scotland could be reduced to half its present figure (Baird, 1947); and if we are in any danger of feeling complacent about Edinburgh's neonatal mortality rate of 26, it is salutary to remember that in Chicago the rate was reduced from 25 to 18 in a period of three years. This is surely a challenge which it would be pusillanimous to refuse.

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## DISCUSSION

*Sir Henry Wade* called for a vote of thanks to Professor Ellis for his most interesting paper, and complimented him on the manner in which he had dealt with the problem from all angles and referred briefly to a few points on the social side of the problem that had been discussed.

*Dr Fakmy* said that, while Cæsarean section reduces enormously the risk of fetal damage in the properly chosen cases, yet an infant born by abdominal section could suffer intracranial hæmorrhage and die thereafter.

In regard to pregnancy toxæmia—while there was some evidence to show that dietary factors play a part, yet it was a well recognised fact that toxæmia occurred irrespective of the social class to which the patient might belong.

*Professor McNeil* said that the whole question of the wastage of infant life was receiving increasing attention, and it was interesting to look back over a period of one hundred years and realise how much progress had been made in the last thirty or forty years. It was a curious fact, however, that one hundred years ago the infant mortality rate was less in Scotland than in England—now the reverse was the state of affairs.

*Dr Martin* referred to a ten year survey she had carried through of still-born and neonatal deaths in the Elsie Inglis Hospital and, in the deaths due to congenital abnormality, the major factor was *spina bifida*. A careful scrutiny of the history of the mothers in these cases had provided no clue to their causation.

She had been surprised at the unexpectedly high number of babies who suffered from shock through Cæsarean births.

*Dr Traquair* referred to retinal hæmorrhages in the newborn. These were usually ascribed to a prolonged second stage of labour. He was interested to know if they also occurred in infants delivered by Cæsarian section.

*Professor Ellis*, replying, said he did not maintain that asphyxia could never produce cerebral hæmorrhage, but that Ford had failed to produce anatomical lesions of the brain experimentally in asphyxiated animals; when cerebral hæmorrhage and asphyxia were found in association in the newborn it was often impossible to say which was cause and which effect.

# THE TRAVEL JOURNALS OF PETER CAMPER (1722-1789) \*

ANATOMIST, ARTIST, AND OBSTETRICIAN

By DOUGLAS GUTHRIE, M.D., F.R.C.S. Ed.

ALMOST two hundred years ago a young Dutchman, newly arrived in London, made the following entry in his diary: "January 5th, 1749. In the morning at eleven o'clock I enrolled in Dr Smellie's course on midwifery for three guineas."

The student, Peter Camper, was a native of Leyden. Born of wealthy parents in this great centre of culture, he received an excellent education, and it soon became obvious that he possessed talent and ability. His fondness for drawing and painting was fostered by the best teachers, his interest in foreign languages was encouraged, and when he took his M.D. degree in 1746, with a thesis on the physiology of vision, he was a well-educated man in every sense of the term (Fig. 1).

Untrammelled by the need to make money, which is the death of many a scientific enterprise, Peter Camper determined to devote some time to post-graduate study. With his customary keenness and enthusiasm he had entered general practice at Leyden and had been especially attracted to the study of obstetrics, although there was no leading exponent of the subject in Leyden at that time, despite its galaxy of talent. Boerhaave had died in 1738 and the fame of Leyden as a medical school was declining, although Albinus in the Chair of Anatomy, Gaubius in Chemistry, and others scarcely less eminent, were among Camper's teachers. Very soon, in the course of his obstetric practice he was faced with what he called "the tragedy of the wedged head." In the previous century, Roger Roonhuysen of Amsterdam had acquired a great reputation by the use of a secret instrument, a lever or vectis, which, it was said, had been sold to him by Dr Hugh Chamberlen, and which, indeed, turned out to be but a single blade of the obstetric forceps. By the time that Camper entered practice, forceps had come into general use although still a subject of violent controversy, and Roonhuysen, with his lever, still had many followers. In two cases Camper had used forceps but had failed to deliver a living child. Baffled and distressed by his experience he was eager for further information. Just then, a Scottish student at Leyden, of whom there were many, told him that in London Dr William Smellie was acquiring a great reputation as a teacher of midwifery.

Peter Camper at once decided to visit England. On 16th December 1748, he embarked in the packet boat at Helvoet, and arrived at Harwich sixty hours later, after a stormy passage. Continu-

\* Address to a meeting of the Edinburgh Obstetrical Society, 10th December 1947.

ing to London by stage-coach, he followed the practice of every learned foreign visitor by calling on Dr Richard Mead, who had studied at Leyden under Boerhaave's predecessor, the versatile Edinburgh graduate, Dr Archibald Pitcairne. Mead possessed not only the best library and art collection but also the most fashionable practice in London. Camper writes, "December 27th, 1748; I went to Dr Mead's and saw an original head of Homer in bronze, paintings of Erasmus by Holbein, of Vesalius by Titian, and many others."

The entry of 2nd January 1749 suggests that Camper had come to London to study art as well as obstetrics; "I was introduced at the Painters' Academy in London and was accepted as a Member at a contribution of two guineas." It seems fairly obvious, however, that the main objective of this first journey to England was to attend Smellie's course of instruction in obstetrics (Fig. 3). "January 21st. Saw Dr Smellie deliver a child with the forceps; the head was slightly bruised and the child alive."

Of course Camper never dreamed, any more than did Pepys, that his diary would be published. He wrote it for his own use, and after the above entry, he breaks off, and interpolates his notes of Smellie's lectures. The notes, though brief, show very clearly the magnitude of Smellie's achievement. Camper's diary, preserved in the University of Amsterdam, was published in Dutch and English, by Dr Nuyens in 1939, but it is not so well known as it appears to deserve.

### THE CAREER OF DR WILLIAM SMELLIE

Before dealing with Camper's notes, however, it may be advisable to remind you of the life and work of his teacher, The Master of British Midwifery (Fig. 2). William Smellie's decision to abandon his country practice in Lanark in order to become an obstetrician in London is one of the most dramatic episodes in medical history.

Of his early life we know little, and that little is derived from the evidence of the family tombstone in Lanark churchyard which tells us of his parentage, of his birth in 1697 and of his wife Eupham Borland who died seven years after him, while his own simple epitaph reads, "This is Doctor William Smellie's burial place, who died March 5th 1763, aged 66." The tomb has been protected by a little chapel, erected by the obstetricians of Glasgow and Edinburgh as a tribute to the great master of their craft.

Although he became M.D. of Glasgow in 1745, there is no proof that Smellie was originally a graduate of any university. It appears probable that he entered the profession by the gateway of apprenticeship, and it has been surmised that he was apprenticed to Dr John Gordon of Glasgow, to whom he refers as "my old acquaintance and senior practitioner in the art of midwifery." There is documentary proof of the fact that Tobias Smollett was apprenticed to Gordon, probably at the same time as Smellie, and it is significant that both Smellie and Smollett went to London in 1739, perhaps even together.



Glaister argues in favour of this idea, and it is interesting to think of Smellie in the company of "Roderick Random." Certainly Smellie's intimacy with Smollett was life-long, and it is also certain that Smollett assisted his friend in the writing of his treatise and that he edited the third volume.

For seventeen years, from 1722 to 1739, Smellie had practised in his native town and neighbourhood. There were then few midwives in rural areas, and the attitude of patient to doctor, and also of midwife to doctor, was more friendly and intimate than it was in larger centres. Accordingly Smellie did not lack obstetric practice, and no less than 62 of the cases described in his treatise were attended during the Lanark days. The unsolved problems of midwifery, and the mortality among infants and mothers, disturbed him sorely. At last, profoundly dissatisfied with the current teaching, he journeyed to London where he soon found "that nothing was to be learned there," and then to Paris where he attended a course on midwifery under Gregoire, who was the first to teach obstetrics at the Hotel Dieu, and who was succeeded by his son. "There likewise I was much disappointed in my expectation," wrote Smellie, ". . . his machine was a piece of basket work, upon which he could not clearly explain the difficulties." Returning to London, Smellie devised his own method of teaching, and he worked out an explanation of the mechanism of labour which was his greatest contribution to obstetrics. "Having lost several children and sometimes the mother, I began to alter my opinion and consult my own reason." Smellie had been in London for nine years when he was visited by Peter Camper, although his famous treatise on midwifery did not appear until three years later. That treatise ultimately extended to three volumes, the second and third consisting of case records. The first volume appeared in 1752, the second in 1754, and the third, edited by Smollett, after Smellie's death, in 1774. There were numerous editions and the work was translated into French, German and Dutch. The treatise contained no illustrations, but these were published separately, in 1754, under the title, *A Set of Anatomical Tables*. Of the forty plates, eleven were drawn by Peter Camper, and the remainder by Rymdyk who also drew the magnificent illustrations of the gravid uterus for William Hunter's monumental work.

Incidentally, it may be remarked that the only known portrait of Smellie, presented to the Royal College of Surgeons of Edinburgh by Mr Harvie, W.S., son of Dr John Harvie who succeeded Smellie in practice in London and who married his niece, is usually regarded as having been painted by Smellie himself. The belief is based upon the statement in Smellie's Will that he bequeath to the Grammar School of Lanark "three pictures, my father's, my mother's, and my own, drawn by myself in 1719." But there is no other evidence of Smellie's prowess as an artist. He made no attempt to illustrate his own writings, and the portrait in question is the work of an expert

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artist. It appears very unlikely that Smellie was an artist, although he may have been an amateur musician, as witness his bequest of "nine English floots" and some music books.

The library which Smellie bequeathed to his native town of Lanark is still preserved there but is seldom visited or consulted. One hopes that some day it may be transferred to an academic centre where it might prove of real value, and not be a mere curio.

Smellie's treatise owes nothing to tradition, but is entirely the fruit of experience. In the preface he tells us that the book was not "cooked up in a hurry" but that it had taken him six years to commit his lectures to paper. Furthermore, he states that "during 10 years I have given 280 courses of midwifery to more than 900 pupils and in that series of courses 1150 poor women have been delivered." He also remarks, "my own private practice hath been pretty extensive." The treatise commences with an excellent historical survey which is still well worthy of study, and which concludes with the words; "We ought to be ashamed of ourselves for the little improvement we have made in so many centuries."

Fifty years ago Smellie had an able biographer in the person of another son of Lanark, Professor John Glaister. Glaister covered the ground most thoroughly, although perhaps he gave too much consideration to the petty feuds of the time, and to the stupid criticisms of Smellie's work. Were he alive to-day, Glaister would be keenly interested in the revaluation of Smellie's achievement in the light of Peter Camper's diary.

#### SMELLIE'S CONTEMPORARIES IN OBSTETRICS

And now, before returning to view the work of Smellie through the eyes of his young Dutch student, it may be useful to mention, very briefly, the position of some of Smellie's obstetrical colleagues. When Smellie went to London, the most fashionable obstetrician (man-midwife to the populace, accoucheur to the intelligentsia) was Sir Richard Manningham. Manningham was the first to establish maternity wards, in 1739, and he achieved fame, or at least notoriety, by his exposure of Mary Tofts of Godalming, who claimed to have given birth to 15 rabbits, and who had gained money and sympathy by her fraud.

John Maubray, author of *The Female Physician*, the first to teach midwifery systematically in England, who practised midwifery from his house in New Bond Street, had died several years before Smellie's arrival. For the most part, midwifery was still in the hands of midwives who called in a surgeon in case of emergency. The man-midwife had not yet acquired a worthy status; he was not eligible for admission to the College of Physicians, and the number of such practitioners was small. This antagonism was less apparent in France, where the midwives were of good education and high status. In Paris there had been schools of instruction for midwives even in the seventeenth century

when Louise Bourgeois was the first midwife to publish a work on obstetrics (1609), she set a standard which was fully upheld in the following century by Maire-Louise La Chapelle (1769-1821) and by her more famous colleague Marie Anne Boivin (1773-1847). In Britain, however, the Sairey Gamps and Betsy Prigs remained a reproach to their calling. Although Smellie suffered at the hands of certain of those midwives, he bore their insults with restraint and dignity, holding that "gentle methods will prevent that mutual calumny and abuse which too often prevail."

When Smellie came to London, Fielding Ould, who also had studied in Paris under Gregoire, had just commenced his distinguished career in Dublin, where he was to succeed Bartholomew Mosse in 1759 as Master of the Rotunda Hospital.

The north of England had a famous obstetrician in the person of John Burton of York, the Dr Slop of *Tristram Shandy*, although in real life he was not quite so grotesque a figure as he is in the novel. His "extractor," you may recollect, slipped on one occasion and knocked out several of his front teeth; it was certainly a much more dangerous weapon than other patterns of obstetric forceps (Fig. 6). As was perhaps natural, he smarted under the satire of Sterne, as well as the indignity of imprisonment as a Jacobite. The failure of his *New System of Midwifery* to achieve a success equal to that of Smellie's treatise, was the last straw, and he attacked Smellie in a lengthy public letter. Some of his criticism was justified but, as so often happens, he went too far, and Smellie, very wisely, paid no attention to his baseless and bitter accusations.

Turning from Smellie's chief critic to his closest friend, there must be mentioned the name of William Hunter who came, also from Lanarkshire where he had shared a practice in Hamilton with William Cullen, to assist Smellie for a time and to reside with him in Pall Mall in 1740. Although somewhat overshadowed by his brother John, William Hunter became eminent as an anatomist and obstetrician, founding the Windmill Street School of Anatomy in 1770, practising as the most fashionable obstetrician of his day, and combining the two branches of medical science in his handsome folio work, *The Anatomy of the Human Gravid Uterus*. Hunter's friendship with Smellie was long and intimate, as is shown by the letters which passed between them, some of which have been preserved.

The fact that Smellie's fame had reached Holland shows that he had acquired a high reputation as a teacher within the first eight years of his residence in London. Returning to Camper's diary as our source of information, we find his recording that "the famous Dr Smellie lectures in English, and usually completes his course in a fortnight, devoting at least two hours daily to his lectures." Camper goes on to describe the obstetric models or "machines," as Smellie called them, each consisting of "a real pelvis covered with leather and a foetus made of wood and also leather covered. The skull bones are

moveable and kept up with springs, the nose is inset, with a spring, the jaw bone jointed and moveable. Likewise, the after-birth is made of leather." "The parts have been made with such remarkable skill that all the necessary functions of parturition are performed by working models."

I must not weary you with too many extracts from Camper's notes of Smellie's lectures, but perhaps a few quotations will suffice to illustrate the nature of his teaching.

#### CAMPER'S NOTES OF SMELLIE'S LECTURES

"Dr Smellie gives the exact measurements of the pelvis and is the first, I believe, to have applied them in practice. He asserts that the Irish man (Fielding Ould), who was the first to describe the oblique descent of the head into the pelvis, threw great light on the problem for him." Camper goes on to record how the head, having entered the pelvis, gradually turns so that its long diameter may correspond with the long antero-posterior diameter of the pelvic outlet, and he gives details of the measurements.

Smellie, himself, had described in his treatise how, in studying the mechanism of labour, he found the key to many obstetric problems. "I surveyed the dimensions and form of the pelvis, together with the figure of the child's head, and from the knowledge of these things I not only delivered with greater ease and safety than before but also had the satisfaction to find in teaching that I could convey a more distinct idea of the art." Deventer of The Hague, a century earlier, had noted the influence of pelvic deformities upon labour, but Smellie carried the investigation much further.

Camper's notes of Smellie's second lecture relate that "he has preserved in spirit the body of a woman who died shortly after delivery, the size of whose pelvis between sacrum and pubis, was diminished to less than three inches. He uses this body for students to insert their hands so that they may accustom themselves to the practice." After dealing with the diagnosis of pregnancy and noting that "exploration with the finger shows no sure signs in the first months," he discusses the connection between placenta and uterus, a problem which also engaged the attention of William Hunter. "A midwife of age and experience, when asked by Smellie why she had not cut the cord, replied that she never did so until the pulse-beat ceased, as this made the infant strong." Smellie also told his class that if a placenta, delivered before the foetus, was kept in warm water, it recovered and the circulation continued, while not a drop of blood stained the water. Nothing was plainer, he affirmed, than that there was no anastomosis between the vessels of the placenta and those of the uterus.

In lecture three, Smellie discusses the vomiting of pregnancy. In his view, no ill is to be feared. "On the contrary it is rather an advantage, and helps to stretch the uterus." Camper adds a note:

"When I heard the Doctor a second time, he did not maintain so strongly that vomiting was good for stretching the uterus. He said, 'Others allege that vomiting stretches the uterus'." In Smellie's view, "Swelling of the labia, so alarming in appearance, seldom obstructs labour," and Camper makes the observation, "I had such a case at Leyden, and the Irish Doctor Macnamara, like myself, feared everything would be torn at the birth," but "Contrary to expectation, there was not the slightest laceration."

Before Smellie's day it was commonly believed that the foetus lay head uppermost in the uterus until the seventh month, and that it "then toppled over, in order," so Burton stated, "to be ready to crawl out into the world on its hands and knees," (Fig. 5). Smellie taught (as we read in lecture four), "that the foetus during the whole period of gestation is placed with the head downwards."

Dealing now with abortion, Camper continues his notes; "Dr Smellie believes that repeated miscarriage is due to the ovum sticking in the neck of the uterus, which cannot expand. The ovum dies and is expelled. Dr Smellie can do nothing to prevent miscarriages; all that he is anxious to prevent is excessive loss of blood."

On the subject of infant resuscitation, Camper notes that, "Some foetuses do not at once start breathing at birth. Smellie relates a case where the accoucheur put his own face next the infant's and inflated the lungs and it at once began to breathe. Dr Hunter had a similar successful case but Dr Smellie has never been successful with the method."

The sixth lecture is of great interest, as Smellie then describes his experience with forceps, which, he says, "should never be used unless there is urgent necessity." To quote again from Camper: "Dr Smellie deals with the use of the fillets, which instrument he regards as dangerous and based on an incorrect idea of the situation of the head in delivery." In his treatise, Smellie mentions that "the fillet of Mauriceau is fixed with much trouble and is, after all, of very little use." He adds that Mauriceau "was ignorant of the forceps," and he also states that Amand's net is "ingenious, but is not applied without great trouble."

It is not necessary, in this paper, to review the story of the forceps, the family secret of the Chamberlens for over a century. In 1735, Alexander Butter of Edinburgh, published his account of Dusée's forceps, (Fig. 4) and this was read by Smellie, who promptly introduced the forceps into his own practice. The blades were not fenestrated, and could be fixed in two positions. When he went to London, Smellie devised the English lock, and he had his forceps made of hard wood, to avoid alarming the patient, and later they were of metal having the blades covered with strips of leather, "to be newly covered every time of using." The pelvic curve, adopted by Smellie, is acknowledged to have been the invention of Benjamin Pugh of Chelmsford about 1750 (Fig. 7). A three-bladed instrument designed by André Levret,



FIG. 1.—Peter Camper, 1712-1789.



FIG. 2.—William Smellie, 1697-1763.

A  
C O U R S E  
O F  
L E C T U R E S  
U P O N  
M I D W I F E R Y,  
W H E R E I N

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tions, to Assist the Judgement and Memory of the Students.

By WILLIAM SMELLIE, M. D.

Printed in the YEAR MDCCXLVIII.

FIG. 3.—Syllabus of Smellie's Lectures, 1748.

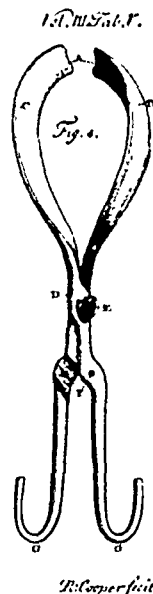


FIG. 4.—Dusée's Forceps, as illustrated  
in the paper by Dr A. Butter, noticed  
by Smellie in 1735 (*Medical Essays  
and Observations*, Edinburgh, 1735).





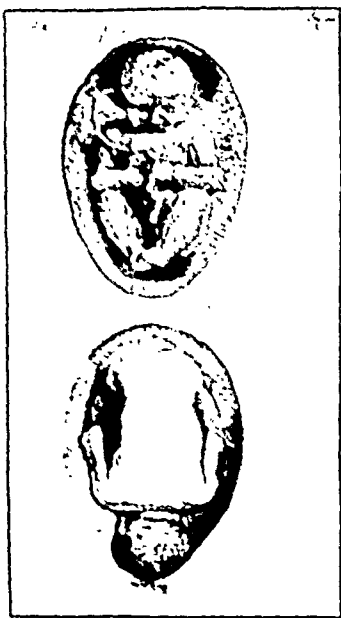


FIG. 5.—Positions of Fœtus in Utero, according to Burton; 1. before; 2. after seventh month.

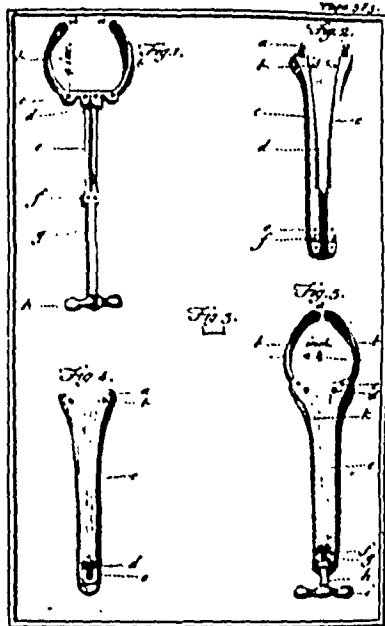


FIG. 6.—Burton's Obstetric Forceps, or "Extractor."

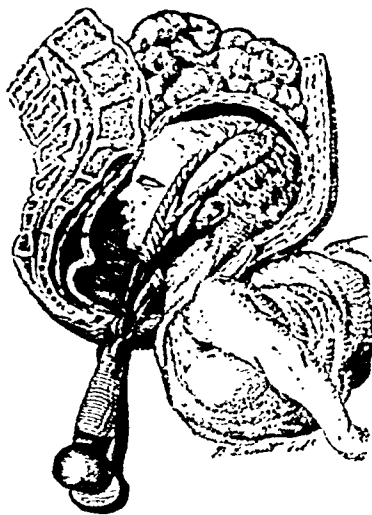


FIG. 401. — Application du forceps de Smellie dans la présentation du siège.

FIG. 7.—Application of Forceps to After-coming Head, as illustrated by Smellie.

part of the os sacrum where it joins the loins; with the occiput put above the brim of the os pubis, and will never be forced by drawing it out in a straight line. Let A-B be the part of the head sticking at A and B. If it is drawn in the straight direction to the operator CD, the head will never be able to be drawn into the pelvis, because all force is lost at A. What then? Insert the finger in the mouth and then by drawing up towards F and then pressing down to G and at the same time working the mouth and head towards the opening of the vulva, the head should be slowly freed until the face sticks in the hollow of the os sacrum and then it is drawn out by drawing up again in the usual way.

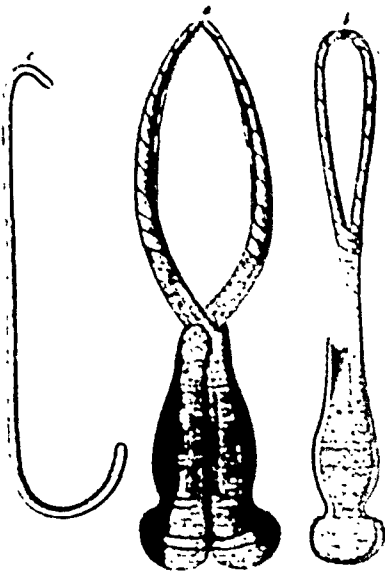
*Note.* It was always my method to free foetuses born as far as this by drawing them towards the lower parts, then the head comes out first by the occiput, and the face follows; but in such a way so as not to undertake the extraction of the head until all the head is in position in the pelvis.



FIG. 8.—Sketch by Peter Camper of Smellie's Method of delivering the Head in Breech Presentation. (Camper's Diary.)



geven, om langs een anderen weg terug te vloeren, dan langs wien zij lag-pooten werd. Deze verbeterde instrumenten werden uit-



A.

B.

FIG. 9.—A. Blunt Hook or Crotchet.  
B. Smellie's Forceps with Leather-covered blades.

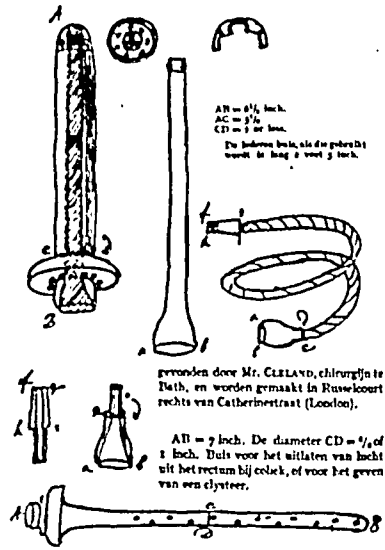


FIG. 10.—Cleland's Apparatus for Injection of the Water of Bath into the Uterus. (Camper's diary.)

# HISTORICAL AND PRACTICAL ENQUIRIES

ON THE SECTION OF THE  
SYMPHYSIS OF THE PUBES,

As a SUBSTITUTE for the  
CÆSARIAN OPERATION,

PERFORMED AT PARIS,  
By M. SIGAULT, OCTOBER 2d. 1777.

By M. ALPHONSE LE ROY,  
Docteur Regent of the Faculty of Physic in Paris, and Professor  
of Midwifery, &c.

TRANSLATED FROM THE FRENCH,  
BY LEWIS POIGNAND,  
Of the Corporation of Surgeons, London, and Surgeon to the  
Widow's Lying-in Hospital.

LONDON:  
Printed for R. BALDWIN, Print-shop-Row,  
MCCCLXXVIII.

FIG. 12.—Title-page of Le Roy's  
Treatise on Sigault's Operation  
of Symphysiotomy, 1778.



FIG. 11.—Drawing by Peter Camper in  
Smellie's *Anatomical Tables* to illustrate  
a Narrow Pelvis and a "Wedged Head."



who was Smellie's counterpart in France, was regarded by Smellie as "a contrivance too complex."

There is no need to repeat Smellie's rules for the use of forceps as taught in his lectures. Suffice it to say that he condemned, "the common way of pulling the head anyhow, with downright violence." His directions are very clear, and he concludes by telling the operator to "wipe the blades of the forceps singly, slide them warily into your side pockets, and then deliver the placenta."

As is well known, Smellie's name is associated with the management of breech presentations, and on this subject Camper's notes are of interest. "When the foetus has been delivered," he writes, "what is to be done if the head does not follow? Direct traction will never free the head. A finger must be inserted in the mouth and then by a rocking movement, up to F and down to G, the head is slowly freed until the face enters the hollow of the sacrum and is then extracted by drawing the body up in the usual way." (Fig. 8).

Camper's notes on version are very brief; probably he was already fully familiar with the technique. Considerable space, however, is devoted to the means of destroying the unborn child, now so fortunately abandoned. Smellie used scissors and a blunt hook for this operation, "to diminish the volume of the foetus when the head is so large or the pelvis so narrow, that it cannot pass" (Fig. 9). It is clear that Smellie had an uneasy feeling that some of those children might have been saved: "The child should never be destroyed except when it is impossible to turn, or to deliver with forceps." The epoch of Cæsarean Section had not yet arrived. Cæsarean Section was performed only after the death of the mother, and Smellie writes: "It ought to be delayed until the woman expires, and then immediately performed with a view to save the child." The leading French authority, Francois Mauriceau, wrote in his Aphorisms in 1739 that, "The Cæsarean Section must never be performed while the mother is living, because it would destroy her." Fielding Ould held similar views. He regarded Cæsarean Section on the living mother as "a detestable, barbarous and illegal piece of humanity," an opinion shared by William Hunter and other contemporary obstetricians. The operation had been performed unsuccessfully by Mr Smith, an Edinburgh surgeon, in 1737 (was this Robert Smith, second Professor of Midwifery, 1739-56?) and successfully by Mary Donally, an Irish midwife, in the following year. Professor Alexander Hamilton of Edinburgh advised it, in 1783, but only as a "dreadful expedient." The first successful Cæsarean Section in U.S.A. was in 1794, when Dr Jesse Bennett, in Virginia, performed it on his own wife; mother and child survived. Craniotomy was preferred until nearly the end of the nineteenth century, when the adoption of Listerian principles entirely altered the outlook. Further consideration of the Cæsarian operation would lead us too far from the present topic.

Smellie's final lecture is devoted to the puerperium and to the care

of the newborn child. Smellie did not stitch a torn perineum, holding that "it is better to leave it to Nature." The infant was to be "washed in thin beer, or in wine and water."

#### CAMPER'S FIRST JOURNEY TO ENGLAND: 1749

Although his notes of Smellie's lectures occupy the greater part of Peter Camper's diary of his first visit to England, there are recorded many interesting episodes. There is, for example, the note of 7th February 1749: "I was taken to Sir Hans Sloane, who is 87 years old, famous for his collection, incredibly large and costly. He lives in Chelsea, and is hard of hearing, but well preserved." On 13th February: "Saw the famous telescope made by Mr Short, belonging to Dr Stephens. We looked at the moon and saw its mountains." Short was a native of Edinburgh who achieved fame as a manufacturing optician in London and who was elected F.R.S.

During the spring, Camper paid brief visits, by stage-coach, to Oxford and Cambridge. At Oxford he notes: "All the University people wear a kind of toga, and square hats, except the servitors who wear a round bonnet." On 15th March again in London, he attended a concert at Covent Garden: "Handel himself played the organ." Three days later he "visited the Tower, and saw two lions, an eagle, and an ostrich  $4\frac{1}{2}$  feet tall not counting his neck."

The entry of 2nd April describes "a visit to Greenwich by water. Was impressed by the King's yacht, beautifully gilt; Greenwich Hospital and the Royal Observatory." Next day: "I dined with Mr Jackson, chemist in Pall Mall who has a magnificent collection of minerals. His mistress, who lives with him, is one of the most beautiful girls I have seen in England." On 7th May, Camper "botanised on Primrose Hill with Welsh and Elliot, two Scottish doctors who had studied at Leyden," and on 10th May, again in medical company, he "sought herbs at Sydenham, a pretty village. On the heath is a well that yields purging water, of which I drank half a pint, and noticed the effect in the evening." A fortnight's tour in the West of England was commenced on 18th May, when, "we setted out" on horseback for Bath, arriving two days later. Camper was much impressed by Bath, by the parade and the ballroom, by the elegant buildings, the Abbey and the fine scenery all round. But he adds, "the baths are very bad, all open and no conveniency at all." At Bath, Camper "dined with Mr Cleland, the famous surgeon, and . . . saw several contrivances (which he illustrates) for the injection of Bath water into the uterus" (Fig. 10), Bristol and the Wye valley were also visited. At Bristol he saw in the square a fine statute of King William, and "was surprised to see that his horse was represented as evacuating excrement." Peter Camper's stay in England was now nearing an end. No sooner was he back in London than he set off on his homeward journey by Canterbury and Dover, then across to Boulogne, where the record ends.

## THE SECOND JOURNEY: 1752

Three years later, Camper made a second journey to England. He was now thirty years old, and as he was now Professor at Franeker in Friesland he could devote only the summer vacation to travel. One of the main objects of this visit was to make some drawings for Smellie. Camper again lands at Harwich, stops the night at Colchester and then posts to London, the journey costing "two guineas, with refreshment."

"On July 14th, I hired two rooms near Dr Smellie, who was the first person I saw, as also his figures, drawn by Rymsdyk in vermilion, on a yellow background." (Now in the library of the Royal College of Physicians, Edinburgh.)

Tuesday, 18th July: "I drew for Smellie, and checked the position of the heads that are wedged (Fig. 11). Wednesday at Smellie's; dined at Hunter's and saw his figures of uterus gravidus, very beautifully drawn by Rymsdyk. I next saw several diseases of bones of which I intend to do drawings, and will therefore not write long. In the evening saw Smellie deliver a woman with forceps. I had examined the case. The operation was done quickly and the child was alive."

The next entry tells of Camper's meeting with Donald Monro, Physician to St George's Hospital, the second son of Alexander Monro (*primus*). "20th July. Professor Monro's son had supper with me and I enquired about the tearing of his father's tendo Achilles. He related to me that his father had danced the Scots measure in 1743 in his own house, and, at the finish, had torn the tendo; that Professor Plummer had torn it, and so had several other people. It is very funny that many have had the same accident in this dance."

The note on 22nd July is also interesting: "I drew for Smellie, and saw a young woman who had for three years had complete prolapse of the uterus. The uterus was right out and the vagina was reversed . . . Smellie easily pushed it in and applied Suret's pessary . . . She walked away quite at her ease."

On 23rd July, Camper breakfasted with Dr William Pitcairn and saw St Bartholomew's hospital. Among the patients was a man with jail fever which he had caught when making a hole for a ventilator in the roof of Newgate prison, as recommended by Rev. Stephen Hales. Another interesting meeting was with Samuel Sharp, who succeeded to the surgical practice of Cheselden. Camper saw Sharp remove a large tumour of the testicle, and he records that the patient died twelve days later. Sharp asked Camper to dinner and they discussed trephining, catheters, the removal of cataract and fracture of the knee-cap.

Next, we find Camper visiting the smallpox hospital, where Dr Archer told him that he had lost only two cases out of 192 inoculations, which he carried out by rubbing as it was safer than making a scratch.



On 27th July, Camper attended a forceps delivery by Smellie, after which "we examined 21 pregnant women, and guessed the time of pregnancy according to the rising of the uterus." A few days later (4th August) he "heard Smellie's lesson on face presentations." He applies the forceps and draws out the head, but guides the jaw with two fingers of one hand, and the forceps with the other, otherwise the jaw catches on the *os pubis* . . . I afterwards saw a good way of washing linen. Most people affirm that it washes quicker and with less soap." This note is illustrated by a sketch of the machine.

There are several references to William Hunter, with whom Camper had many interviews. On 12th August he spent the morning with the engineer, John Smeaton, famous as the designer of Eddystone Lighthouse, who showed Camper his air pump and his compasses, and discussed the various methods of ship-building.

The only excursion of any length on this visit to England was a tour to Worcester and Ludlow. There Camper fell ill, and "was bled by Phillips, a Tory surgeon." He was at the time the guest in a Tory household, whose members would rather die than be attended by a Whig.

Returning to London, Camper had interviews with Dr Knight, librarian of the British Museum, with Dr Fothergill, who was using fluid from the tanneries as a dressing for Scorbutic ulcer, and, of course, with Dr Smellie. He bade farewell to his London friends and returned to Holland early in September.

After Smellie and Camper thus parted in 1752, each continued to lead a busy life in his own sphere. In 1759, Smellie retired from practice and returned to Lanark, where he had a small estate close to the town with a house which he had built and named Smellom, or Smyllum. In recent years it has been enlarged and has been in use as an orphanage.

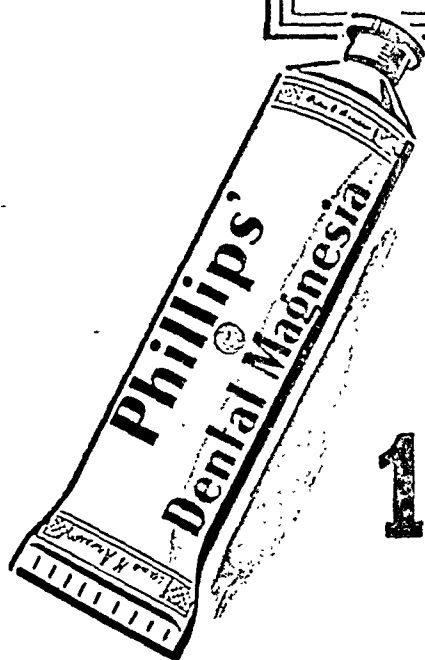
Of the later period of Smellie's life little is known, but there is a letter in the Hunterian Museum of Glasgow which shows that he had a gift of humour. It seems that before he left London, Smellie had some difference of opinion with William Hunter, and their mutual friend Dr Clephane had suggested that they should meet in a Coffee House to settle their differences. This meeting never took place, but Smellie replied to Dr Clephane in a letter purporting to come from the next world.

He dated his letter, "Shaw Park, near Tartarus, Era of Chinese Pluto, 41758," and he writes: "Some posts ago I wrote you in a hurry a little scrawl from the other world, and since you have no good body daying to bring an answer, I send a long one to plague you like an infernal spirit. This way I thought safer after retiring to the gloomy regions, than to have met in the Coffee House . . . to prevent blood and battery which perhaps would have obliged me to have kept wandering 100 years before the boatman would receive me.

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Smellie died at Lanark four years later. The London practice had meantime passed into the hands of Dr John Harvie who had married Smellie's neice, and Harvie continued to hold it until his death in 1770. Harvie deserves to be remembered as the first to advocate expression of the placenta, a hundred years before Crédé. There is an interesting letter in the University Library of Amsterdam from William Hunter to Peter Camper, regarding the disposal of Smellie's property. The letter is dated 1778, and Hunter writes : " I have twice had the pleasure of a letter from you since I wrote you last which was upon the death of Dr Harvie, to let you know that all Dr Smellie's apparatus was to be sold. I thought that you or your friends might wish to have some of them. I bought several, particularly the original drawings." Hunter goes on to refer to two pupils sent to him by Camper, and he discusses the natural history of the rhinoceros, and inscriptions on Roman coins. His concluding sentence reads : " I am sorry for the sake of some of your works that I cannot read Dutch ; but already I know enough of you to be, with very high esteem, most faithfully yours, William Hunter."

#### THE THIRD AND LAST JOURNEY : 1785

Many years passed before Peter Camper visited England for the third and last time. Meanwhile he had a very busy life. He was now a man of eminence and high reputation. From the Chair at Franeker, he had gone, in 1755, to be Professor of Anatomy and Surgery at Amsterdam. There he married the wealthy widow of a burgo-master, Madame Vosma, and with her he lived very happily until her death twenty-one years later. He had three sons, Jacob, Pieter and Adriaan ; Jacob accompanied him on the third journey to England. In 1763, he accepted the Chair of Anatomy, Botany and Surgery at Groningen, and in 1776 he retired and went to live in Friesland. The last few years of his life were spent at The Hague, where he was obliged to reside, as a member of the State Council, and where he died in 1789.

Peter Camper's writings were many and varied, as might be expected from the pen of one so versatile. Perhaps his chief interest was in the application of anatomy to art, and his work on this subject is still of great interest. He had a mind like that of John Hunter, keenly interested in all the works of Nature. Like Hunter, he found large animals attractive, and he wrote a Treatise on Whales and another on the muscles of the Elephant. His name is still associated with the facial angle in man which he described. He also wrote on legal and on veterinary medicine, on inoculation, on stone and on hernia, besides a number of papers on archæology. One of his most popular works was a little book, *On the Best Form of Shoe*, (1781),

which was translated into English and French. His chief original contribution to obstetrics was a defence of symphysiotomy.

In 1785, at the age of sixty-five, restless and melancholy since the death of his wife, Camper sought solace in travel and paid his third visit to England. At least one motive for that visit was a desire to ascertain the attitude of English obstetricians to the operation of symphysiotomy. He had heard of Sigault's discovery. Who, indeed, could fail to learn of an operation which won such high approval from the French Academy that they had issued a medal to mark the event? Sigault's first opportunity to perform the operation did not occur until 1777, ten years after he first suggested it. The report states that when he cut through the symphysis, the pubic bones separated with a loud crack, and within five minutes the child was born alive.

The patient was one Madame Souchot, aged twenty-eight, whose previous four labours had been all "very bad on account of her deformity and short stature, which was only three feet eight inches high." After the operation, Madame Souchot had rather a slow and stormy convalescence, but on the 60th day she walked downstairs and was driven in a coach to the College of Physicians, where she "was able to return thanks for favours received from the greatest part of that respectable body." The good lady found herself one of the famous patients of history. Sigault, assisted by Le Roy, had achieved a triumph indeed, and the Academy did not wait for further evidence before bestowing their lavish praise and award. In the view of the Academy, it was "one of the most important discoveries of the age."

Long before then, in 1769, after the operation had been suggested, but before it had been practised, Peter Camper made the experiment of dividing the symphysis in a pig. The pig having recovered, he went a step further and sought permission to operate upon a woman who was to be executed for child murder, but the request was refused by the Government. Alphonse Le Roy, in his book, *Historical and Practical Enquiries on the Section of the Symphysis of the Pubes as a substitute for the Cæsarian Operation performed at Paris by Monsieur Sigault, October 2nd, 1777*, refers to Camper's work in the following terms :

"While the French surgeons were disputing this matter, Mr Camper, a Dutch physician, had recourse to experiment. He performed this operation on a sow, after she had littered; she continued to suckle her pigs, to eat, drink, and walk, and though she threw off the bandage which had been applied in order to favour a union of the parts, they were healed in 15 days. The experiment, being made known throughout Europe, decided one of the chief points in question, viz., the reunion of the parts, but it said nothing respecting the separation, and gave no answer to the objection made to its efficiency." (Fig. 12.)

Nevertheless, Camper, when he came to England in 1785, was able to quote six cases in support of his thesis; all the mothers re-

covered, and three children were born alive. He hoped to convince his English colleagues that at last an effective solution to the problem of the "wedged head" had been found.

By this time, Smellie and William Hunter were both dead, and most of the practice and teaching of Midwifery in London had passed into the hands of Thomas Denman (1733-1815) and William Osborn (1736-1808). In 1783 Osborn had published an essay on symphysiotomy (with notes of 25 cases known to him). It was, he said, "in no circumstances a warrantable operation." Although less dangerous than "that most fatal operation, Cæsarean section," it was equally unnecessary. Osborn's Essay eventually formed about one-third of his book, published some years later, *Essays on the Practice of Midwifery*, 1795. Denman was also opposed to symphysiotomy, an operation which, he said, "could not be adopted in London because the husbands would never permit it."

Osborn's Essay is of special significance, as he gives a detailed discussion of symphysiotomy, relating all the known cases and writings, although, curiously enough, he seems to have had no personal experience of the operation. It appears to have been the subject of many a heated debate at the end of the eighteenth century. One of the few who favoured symphysiotomy in England was John Leake who wrote an *Introduction to Midwifery*, in 1777, but he, too, had failed to make a practical test of the operation. Hamilton of Edinburgh, in his *Outlines of Midwifery*, stated that symphysiotomy was "in no case a justifiable operation."

During his visit to London in 1785, Camper arranged an anatomical demonstration to show "how easy it is to perform the *sectio ossis pubis*." Neither Denman nor Osborn attended, and the audience consisted of their pupils. Camper must have been satisfied when he wrote in his diary that "the lesson passed to my great satisfaction." The only supporter of symphysiotomy among the older practitioners was Robert Blaud, but he told Camper that "in this country they prefer to sacrifice the child."

Apart from this discussion on symphysiotomy, there is little of obstetrical interest in Camper's diary of his third journey to England during the months of October and November, 1785. He again disembarked at Harwich, and completed the journey to London by post chaise at a shilling a mile. With his observant eye he notes that in East Anglia the cattle are hornless and that they do not butt each other. Arrived in London, he spent much time in drawing specimens at the Royal Society and the British Museum; the latter he describes as "a vast collection covered with dust and arranged in no order." He also met John Hunter, who "lookes old and spoke very positively, being accustomed to be first in his art," and a few days later he "visited Mr Hunter's wonderful collection of rare things," and discussed the anatomy of the elephant, a subject which had attracted them both.

The visit to London was not all work and no play. On 20th October he records that "we went to Drury Lane Theatre to see Mrs Siddons, who is surely the best actress I have seen," and on the 22nd Camper "went with Dr Herschel to Windsor," by special coach, three hours from London, "to see his large twenty foot telescope which is able to magnify 6000 times."

He was entertained to breakfast by Dr Lind, "who showed some beautiful Chinese drawings," but who does not appear to have discussed his famous *Treatise of the Scurvy*.

On 27th October, Camper and his son set out on a tour, which included Oxford and Blenheim Palace, where he sketched the bridge. They arrived at Birmingham on 1st November, "a dirty town, full of factories, and with bad roads, not paved." A whole day was devoted to the fire-engines of Mr James Watt, the distinguished engineer. They also met Dr Withering, who stated that half the deaths between fifteen and forty years of age were caused by consumption. He said, too, that the decreased incidence of stone in the bladder was not due to drinking tea. Digitalis was not mentioned, although it was in this year, 1785, that Withering published *An Account of the Foxglove*.

After returning to London on 8th November, Camper was installed, by Sir Joseph Banks, as a member of the Royal Society, and the last entry in the *Journal*, dated 30th November, describes an anniversary dinner of the Royal Society at which many famous men were present, including Sir Joshua Reynolds, to whom Camper had the honour of showing his drawings of facial characteristics in various nationalities.

Here, the *Journal* breaks off abruptly, and there is no record of the return journey to Holland. One only wishes that Peter Camper had visited Scotland; he would have given a graphic account of the condition of medicine and science at that time. Although his is not one of the familiar names of medical history, he deserves to be remembered for his services to art and archæology, to anatomy and surgery, and, above all, to obstetrics, as one of William Smellie's most distinguished pupils.

In conclusion, I should like to acknowledge my indebtedness to Professor Miles Phillips, who originally drew my attention to Peter Camper, and to some of the works to which reference has been made in this paper.

Since the above address was delivered, it has been brought to my notice by Professor Phillips that the original drawings made by Peter Camper to illustrate William Smellie's work, are in the library of the Royal College of Physicians of Edinburgh. They were presented in 1856 by Dr J. G. M. Burt, who later became President of the College.

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## PETHIDINE IN LABOUR \*

By DONALD BEATON, F.R.C.S.Ed., M.R.C.O.G.

SINCE pethidine hydrochloride was first used in labour seven years ago there have been published more than twenty investigations into its benefits, limitations, and indications.

The history and chemistry have already been adequately described, particularly by Gallen and Prescott,<sup>1</sup> and the problem of the pharmacology of the drug is outwith the scope of this communication.

Most investigators used pethidine in combination with some other drug either in part or the whole of their series<sup>1,2,6,7,8</sup> and very few seem to have compared its effects with a series of simultaneous controls—a plan which would seem to be essential in estimating at least the effect on duration of labour.

There have been, on the other hand, only four reported series in which pethidine was used alone. Three of these used no controls,<sup>2,4,5</sup> and Barnes<sup>9</sup> in a series of 500 admits to a selection of cases which seemed more suitable for the use of pethidine, but states, "Ideally, of course, for the purpose of such a series pethidine should be given to alternate primigravidæ in labour."

In assessing the value of a new drug, whether clinically or experimentally, it would seem preferable to use that drug alone and not to obscure its effect by the concurrent use of another. This is particularly so in the use of pethidine, the effect of which on the duration of labour is still under review and its pharmacological action in labour still undecided.

It is also important, in assessing its value, that the element of chance is excluded as far as possible so that this may have a minimum effect on the results.

In writing of this, Professor Bradford Hill<sup>12</sup> points out that "in the interpretation of figures which are at the mercy of numerous influences" (and no one will deny the many influences affecting the parturient) "it is necessary to determine whether individual influences can be isolated and their effects measured. In experiments involving the treatment of a number of patients, who are to be compared with controls not given the specific treatment, any deliberate choice of individuals to be treated may lead, unconsciously, to the treated group differing from the untreated group in some characteristic, which, known or unknown, has an influence on the results. If a series of cases is large a random allocation of individuals (*e.g.* alternate cases) may reasonably be relied upon to equalise the groups in all characteristics except that under examination. Such a method of allocation does *not* obviate the necessity of testing, in the statistical analysis of

\* Read at a meeting of the Edinburgh Obstetrical Society on Wednesday, 14th January 1948.

the results whether, in fact, groups are equal in all characteristics which are believed to be relevant."

I can find only two series which conform, for the most part, to Professor Bradford Hill's requirements.<sup>9,10</sup>

It appears reasonable, therefore, that a series be investigated with optimal control and minimal selection and correction while the results are subjected to critical statistical analysis. The number of cases should be at least 1000 including controls.

Method and results should be reviewed in a pilot survey early in the series to give preliminary information as to the value of the investigation and to see if the methods could be improved.

This present communication is such a pilot survey.

In planning this investigation into the clinical effects of pethidine in labour I have decided upon the following criteria: (a) the patients were all primigravidae who were at least thirty-eight weeks pregnant: (b) every alternate primigravida received pethidine as a routine measure and the remainder were not so treated, but may have had some other medication or none at all: (c) patients who were admitted in the second stage of labour were excluded from either group.

All pethidine cases were examined vaginally to determine the degree of dilatation of the cervix, while controls were not so examined unless there was some obstetric indication (this, I now think, is an error which will be discussed later).

The dosage is rather larger than most previous writers have advocated, but has been recommended by Gallen and Prescott<sup>1</sup> and by S. J. Cameron.<sup>11</sup> 200 mgm. of pethidine is administered intramuscularly by injection as soon as the patient is having regular uterine contractions, but rarely before the cervix is 2-3 fingers dilated. If it becomes apparent that the patient is not nearing the second stage of labour within four hours of this first injection (for the effect of 200 mgm. seems to last as long as that) a second dose of 150 to 200 mgm. is given. Trilene analgesia was given to all patients during the completion of the second stage of labour.

### CLINICAL RESULTS

Ninety pethidine cases and 90 controls are now available for study, having been delivered at the Cresswell Counties Maternity Hospital within the past six months.

The total dosages of pethidine were as follows:—

51 patients received 200 mgm.

5	"	"	300	"
10	"	"	350	"
18	"	"	400	"
3	"	"	500	"
1	"	"	600	"
1	"	"	800	"
1	"	"	1000	"

Thus a single injection of 200 mgm. proved sufficient for 57 per cent. of patients and a further 33 per cent. only required two.

Ante-natal complications are shown in Table I and none of these can be said to have influenced either pethidine or control groups

TABLE I  
*Ante-natal Complications*

		Pethidine.	Control.
Pre-eclamptic toxæmia . . . . .		5	5
Eclampsia . . . . .		1	0
Accidental A.P.H. at 36 52 . . . . .		1	0
Hydramnios . . . . .		0	2
Pulmonary T.B. . . . .		0	1
Diabetes Mellitus . . . . .		0	1

except that in one case of hydramnios (control series) labour was prolonged and complicated by retained placenta. A case of eclampsia (pethidine series) was delivered by forceps solely on account of this complication.

The method of delivery is shown in Table II. The only significant difference between the two groups is found in the forceps rate where

TABLE II  
*Method of Delivery*

	Pethidine.		Controls.		Difference.	S.E.*
	Total.	Per cent.	Total.	Per cent.		
Spontaneous vertex presentation	78	86.6	73	81.1	5.5	...
Forceps . . . . .	10	11.1	13	14.4	3.3	0.94
Breech presentation . . . . .	1	1.1	4	4.4	...	...
Cæsarean section . . . . .	1	1.1	0	0	...	...

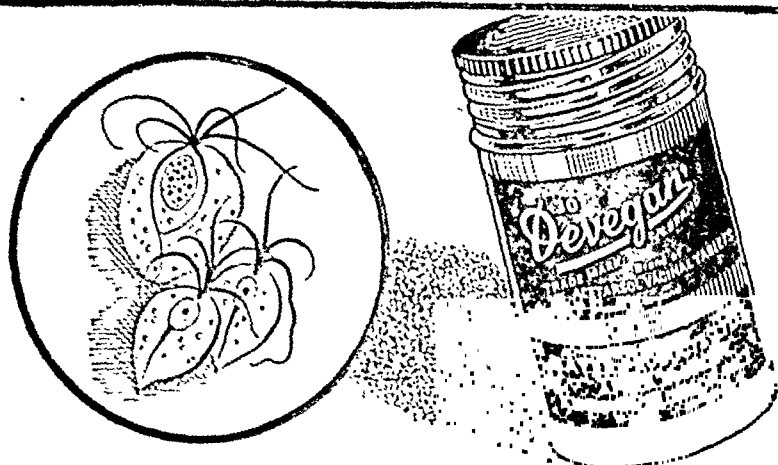
\* Standard error of the difference.

an increase in the control group of 3.3 per cent. is statistically significant and might suggest that pethidine has facilitated delivery.

TABLE III  
*Complications Arising in the Third Stage of Labour*

	Pethidine.	Controls.	S. Error.
Post-partum hæmorrhage . . . . .	6	3	0.35
Retained placenta with hæmorrhage . . . . .	1	2	...
Manual removal of placenta . . . . .	1	0	...

A summary of the complications arising in the third stage of labour is shown on Table III. Post partum hæmorrhage, in varying degrees of severity, occurred twice as frequently in the pethidine series as in



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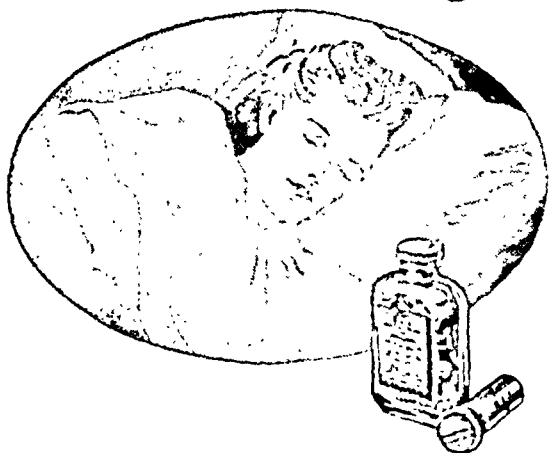
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the control series. This may be of some significance and has not, so far as I am aware, been reported by any previous writer. These cases of post partum hæmorrhage were not associated with any other complications before or during birth. It will be noted later that the average duration of the third stage of labour was not prolonged as compared with the control group. In both groups the majority of these hæmorrhages occurred before the birth of the placenta.

The routine management of the third stage of labour in both pethidine and control series involved the administration of 0.5 m.l. of pituitrin by intramuscular injection immediately after the completion of the second stage.

In an analysis of all these features of labour the numbers are too small to carry any great conviction. The standard errors have been calculated in each case but are only mentioned where they could show a possible significance.

### EFFECT OF PETHIDINE ON DURATION OF LABOUR

Much has been written on this aspect of the problem, and opinions are firmly divided as to whether pethidine has any effect on the duration of labour, though recently Barnes<sup>9</sup> found a significant increase in the first stage from 22.2 hours to 29.5 hours—a difference of 7.3 hours.

Rose<sup>10</sup> made two attempts to assess the effect of pethidine on the duration of labour but could come to no definite conclusion.

TABLE IV

*Analysis of the Duration of the Three Stages of Labour*

	Total.	1st Stage. Hours.		2nd Stage. Minutes.		3rd Stage. Minutes.	
		Mean.	S.D.	Mean.	S.D.	Mean.	S.D.
Pethidine . . . .	90	19.85	17.55	176	159	27.93	36.3
Controls . . . .	90	18.32	13.56	171	143	27.91	61.6
Difference . . . .	...	1.53	...	5	...	0.02	...
Standard error of differences .	...	2.84	...	...	...	...	...

An analysis of the duration of the three stages of labour is shown in Table IV and from this it will be observed that there is no significant difference between the two series; this is to say, pethidine does not appear to hasten labour in the unselected primigravida. This is contrary to the findings of Gilbert and Dixon<sup>3</sup> and of Schumann<sup>7</sup> and particularly of the first investigators in the field Sonnek<sup>2</sup> and Benthin,<sup>4</sup> none of whom appear to have subjected their results to statistical criticism.

In the present series I have taken the onset of labour, for the

purposes of timing its total duration, to coincide with the patient first becoming conscious of intermittent contractions, but I now feel that all clinical signs of the onset of labour and their relation to actual progress of the mechanism of labour must be viewed with reservation. The only reliable index of progress is the degree of dilatation of the cervix, and for this reason it has been decided to examine in future the control cases vaginally to estimate cervical dilatation in the same way as pethidine cases heretofore. In this way the two groups will be much more comparable.

The pethidine series has been subdivided according to the degree of dilatation of the cervix at the time when the drug was first administered. An analysis of the time intervals to delivery (Table V), suggests that these cases, 4 in number, which were given pethidine before two fingers dilatation (and who had been having regular uterine contractions for some hours previously) all had prolonged labours. Two of these ended in spontaneous delivery, one a difficult forceps for persistent occipito-posterior. In the fourth case the cervix failed to dilate more than 4 fingers after seventy-two hours in labour, despite the presence of uterine contractions, necessitating delivery by lower segment Caesarian Section. This patient received a total of 800 mgm. of pethidine and neither she nor the baby showed any ill effects. These were, in fact, cases of inco-ordination of the uterine musculature which did not appear to be affected by pethidine. This is contrary to the findings of other observers,<sup>1, 3, 6</sup> but these few cases do not permit of more than cautious comment.

TABLE V

*Analysis of the Total of First and Second Stages of Labour in Respect of the Degree of Dilatation of the Cervix at which Pethidine was First Administered*

Degree of dilatation . . . .	1 Finger	2 and 3 F.	4 and 5 F.	$\frac{1}{2}$	$\frac{3}{4}$
Average interval in hours between pethidine and delivery	60.5	20.15	18.9	16.5	20.0
Number of cases . . . .	4	51	14	11	10
Standard deviation . . . .	14.8	13.9	9.1	6.0	11.2

It has been suggested that the too early administration of pethidine may upset the progress of labour, and Cripps, Hall and Haultain<sup>6</sup> note that 9 out of their series of 102 cases went "completely out of labour even when they had evidently been in good labour previously."

The current belief that the optimal time to give pethidine is at two fingers dilatation has not been confirmed. The sub-group with the shortest total duration of first and second stages (Table V) was that in which pethidine was given at half dilatation.

In the pethidine group there were 5 patients over thirty-five years of age, whose average duration up to the end of the second stage of labour was 20.7 hours; in the control group there were 10 similar

cases with an average of 30.1 hours. This difference of 9.4 hours (standard error 9.1) is not significant.

### EFFECT OF PETHIDINE ON THE MOTHER

There was no maternal mortality. The analgesic and amnesic effects were estimated from the patient's own observations and the clinical picture. Considerable stress was laid on the patient's observations since the aim of seeking the ideal method for the relief of suffering in childbirth is to achieve that happy state where the mother can look back on her labour with satisfaction unsullied by painful memory.

Out of the 90 patients studied, 12 (13.3 per cent.) claimed complete relief from pain during the whole labour; 69 (76.6 per cent.) felt distinct relief from pain; 2 found no effect. Fifty-two patients (57.7 per cent.) slept between their contractions and 82 (99.1 per cent.) had considerable drowsiness. Fifty-four (60 per cent.) felt themselves effused with a feeling of efficiency and well-being not amounting to euphoria. There were only 2 patients who did not have definite relief either from pain or anxiety, or from both.

The main effect of the larger dosage on the mothers appears to be the relief from nervousness, over-excitement, and anxiety; the decreased pain and the langour was associated with considerable amnesia.

Clinical observation confirmed the above subjective phenomena, there being only 16 patients (17.7 per cent.) who appeared to have slight relief from pain.

No patient became inco-operative and all were easily roused when it became necessary for the patient to co-operate towards the end of the second stage of labour. These observations compare favourably with those of other writers with possibly an increased proportion of patients who experienced good relief from pain and a substantial increase in the degree of amnesia.

The apparent effect of pethidine on uterine contractions is to decrease both frequency and intensity. This appeared to happen in 60 patients (66 per cent.) but it cannot have interfered with the function of the uterus since, in this series, labour was not prolonged. In only 5 cases did frequency and intensity appear to be increased. In 25 cases (27.7 per cent.) there appeared to be no change. In no case did uterine contraction cease altogether after the administration of pethidine.

There were no toxic effects of any moment. Vomiting occurred with some nausea in a third of the cases but both were invariably transitory. A few cases had mild dizziness or sweating, but none of these symptoms caused the patient any alarm or prolonged discomfort and were well offset by the customary sequelæ of a pleasant sensation of warmth and of wellbeing.



## EFFECT OF PETHIDINE ON THE BABY

Of the 90 babies in the pethidine group, 4 were stillborn (4.4 per cent.):—

- (1) A macerated foetus which had died some time before labour started.
- (2) A hydrocephalic foetus, delivered after craniotomy.
- (3) Normal delivery. The foetal heart ceased ten minutes before birth and more than nine hours after the last injection of pethidine. This baby had a very short cord and it is considered that this was the probable cause of stillbirth.
- (4) Here the foetal heart ceased three hours after the first injection of 200 mgm. of pethidine. No obstetric or foetal cause could be found for this.

In the control group 1 stillbirth occurred (1.1 per cent.). The foetus was macerated, the foetal heart-sounds having disappeared some days before the onset of labour.

One stillbirth, therefore, cannot be dissociated from the administration of pethidine but it is not statistically significant.

There were 2 neonatal deaths (2.2 per cent.) but it is not considered that pethidine contributed in any way to these deaths. Two similar neonatal deaths occurred in the control group (2.2 per cent.).

Eight babies at birth in the pethidine group were in a state of blue asphyxia, and 9 in the control series. None of these gave any cause for anxiety and all recovered without complications. There was a greater number of oligopnoeic babies in the control group. There were no cases of white asphyxia.

Pethidine was administered less than two hours before delivery in 4 cases, within three hours in 10 cases and frequently within four hours. None of the babies in these cases showed any greater incidence of respiratory depression than the average for the pethidine series. This is not comparable with the control series since the giving of opiates so late in labour is avoided.

Of the babies who were born alive, therefore, the advantage is with those of the pethidine group. This is in agreement with other writers who stress the benefit of pethidine medication to the baby in comparison to morphine, barbiturates, and "twilight sleep." <sup>5</sup>

## CONCLUSIONS

I set out in this survey to see if there would be value in extending this series and if the methods could be improved.

I propose to continue because certain features have been found which are contrary to the findings of other observers. The method will be altered the better to assess the duration of labour, necessitating vaginal estimation of the degree of dilatation of the cervix in both groups, pethidine and control. Since there was no puerperal morbidity

in either group in the pilot survey, it is suggested that routine vaginal examination is not detrimental to the patient, although contrary to the practice of this hospital.

Hereafter the administration of pethidine will be postponed till the patient is beginning to complain of pain and not before the cervix is 2-3 fingers dilated, otherwise the plan remains unchanged.

Most of the impressions gained, some of which have been tentatively confirmed by critical analysis, have been in accord with the findings of previous writers except that pethidine does not appear to shorten labour.

It has no serious ill-effects on mother or child except that the incidence of post-partum hæmorrhage appears to be increased.

In this series the drug has been used with great advantage to the mothers, particularly those who were nervous and excited. There appears to be safety in large dosage no matter at what time in the first stage of labour the drug is given.

Finally I would like to record my gratitude to Dr Bruce Dewar for permission to publish these cases which were all under his care, and for his encouragement and assistance in preparing this communication. I am also very grateful to Dr Arthur Bethune for his assistance with the statistical analyses and would record sincere thanks to the Labour Theatre Sisters and Nurses for their ready co-operation and helpfulness.

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# THE PLACE OF PARANOID STATES IN PSYCHIATRIC CLASSIFICATION WITH SPECIAL REFERENCE TO PARANOID SCHIZOPHRENIA

By G. D. FRASER STEELE, M.D.

INTRODUCTION.—It has been observed that difficulties have been encountered in the past in deciding which cases presenting paranoid symptoms were justifiably to be regarded as expressions of schizophrenia.

The accurate classification of such paranoid states is of more than academic interest. It has been said that diagnosis between the various members of the schizophrenic-paranoid group is a futile proceeding unless it involves a forecast at least in terms of statistical probabilities of recovery and terminal state (Mapother, 1921). It is here suggested that a clearer understanding of these paranoid states would help towards this goal.

Paranoid schizophrenia has been described as a disorder which appears commonly between the ages of thirty and thirty-five years. It is characterised by persecutory, depressive or grandiose delusions of a changeable unsystematised nature together with similar hallucinations. The course is generally considered to be a steadily progressive one involving considerable personality disintegration and general deterioration.

At the Royal Edinburgh Hospital for Nervous and Mental Disorders, large numbers of patients with symptoms corresponding to this disorder were personally examined, followed up and re-assessed. In addition, carefully documented case records of many others were studied.

This investigation was carried out in an endeavour to decide whether or not the so-called paranoid states of schizophrenia are more closely allied to the paranoid reaction type or to the schizophrenic reaction type.

In this short abstract two representative cases only are detailed and discussed. In the general discussion relevant material from a further ten cases is incorporated.

HISTORICAL NOTE.—From Hippocratic times until the death of Galen when clinical observation was acute and psychiatric thought active, many attempts were made to classify psychiatric material. Thereafter this era of psychiatric wisdom ended and for the next sixteen centuries demonology dominated most conceptions of mental illness.

The beginning of the nineteenth century marked a re-awakening of interest. This followed more exact clinical and pathological investigations and a basis was laid for a more rational sub-division of cases. The approach again became Hippocratic in that observations were directed particularly to the form, course, and outcome of the disease. At the close of the nineteenth century Kraepelin (1919 and 1921) made an outstanding contribution to psychiatry when he formally classified mental disorder, on a symptomatological basis. Starting from what appeared to be an ill-defined and heterogeneous mass of psychotic material he separated the manic-depressive states and divided the residue into three broad groups namely, dementia præcox, paraphrenia and paranoia. The term dementia præcox which was probably synonymous with Clouston's (1904 and 1911) secondary dementia of adolescence had been first

introduced by Morel in 1860. Its initial symptoms became manifest at the adolescent period and it was thought to progress to a terminal state of dementia. Kraepelin further sub-divided the dementia præcox cases into the simplex, the catatonic, the hebephrenic and the paranoid types.

Prognostically this was a classification of the greatest value, since the outcome in the manic-depressive states was usually favourable, while in the others it was considered to be much more variable and less hopeful.

Regarding dementia præcox, paraphrenia and paranoia, Kraepelin freely admitted that his attempt to so group these cases was a tentative one, based principally on the course of the illness. Thus, he thought that 40 per cent. of them ultimately reached a stage in which they presented a characteristic terminal dementia. The paraphrenias constituted a larger group which, throughout their course, showed a better level of personality integration. A small residue he believed to be the real paranoias which showed little personality deterioration and were characterised by fixed systematised delusions and the absence of hallucinations.

It became increasingly clear, however, that neither a terminal state of dementia nor an onset in adolescence were essential features of the symptom complex called dementia præcox.

It was in 1911 that Bleuler approached functional mental disease from the psychological angle and introduced the term schizophrenia. He believed that all such conditions as dementia præcox, paranoid states, paranoia and hallucinosis were but varying manifestations of one underlying process and that for all there was a common constitutional predisposition. The splitting of the intrapsychic functions as he conceived it did not necessarily end in dementia and might arise in adult life. Such a comprehensive term allowed widely varying prognoses in those so afflicted.

Kraepelin was accused of attempting a finer differentiation of these states than the facts allowed when he separated schizophrenia (dementia præcox) from paraphrenia and paranoia.

Like Bleuler, Mapother (1921), believed in the essential unity of schizophrenic and paranoid states and spoke of them in terms of "the schizophrenic-paranoid series," believing the psychoses classified within these categories to form a continuously graded series in which the difference was one of degree and not of kind.

Fifteen years after Kraepelin's statement that there existed a specific disease called dementia præcox, Adolf Meyer (1906 and 1913) made his contributions which threw fresh light on this complex problem of classification. In his psychobiological formulations, the essence of which was a genetic-dynamic approach, he believed that mental illness arose as a reaction of individuals predisposed in a variety of ways to the problems of their lives, and held that a clear understanding of neuroses and psychoses could only be derived from a study of biography and total personality-reactions.

There followed the pre-psychotic personality studies of such workers as Kretschmer (1934), on the Continent, and Amsden and Hoch in America. Hoch (1913) studied the pre-psychotic personalities of a series of cases of dementia præcox and found that certain character traits regularly recurred.

Sharply defined borders for the classification of mental disorder did not appeal to Meyer, and the psychobiologists' criticism of the Kraepelinian formulation was clearly stated by Macfie Campbell (1935), when he wrote, "The Kraepelinian formulation seems to draw rather definite boundaries

where no boundaries exist. It gives the appearance of certainty in regard to prognosis which the facts hardly warrant. The personality receives scant attention. The life situation is considered to be more or less irrelevant. . . . There seems no sound reason for basing the interpretation of a group of cases on a study of the more severe cases and of the later stages, unless these cases and these stages demonstrate the presence of some definite factors of unequivocal nature, which in retrospect throw light on the earlier phases of the disorder." He believed that types of reaction or mental mechanisms were not specific for any mental disorder, but were general characteristics of the human personality, more marked in some individuals than in others, and suggested that what we had to do was to group cases together which had a certain degree of similarity, and, by studying these groups, separate what was individual and incidental from what was general and essential. These comments were directed particularly to the schizophrenic and paranoid psychoses and it is in the classification of these states that lack of agreement is especially apparent.

Following Meyer and his emphasis on the fact that mental disorders were the manifestations of the reactions of specifically endowed personalities to environmental stresses and strains, Henderson and Gillespie (1946) have divided this material into the schizophrenic and the paranoid reaction types. In the former category they included, until recently, the four sub-groups described by Kraepelin, namely the simplex, the catatonic, the hebephrenic and the paranoid forms, and in the latter the paraphrenias and paranoias.

The place of the so-called paranoid states of schizophrenia has for a long time constituted a problem. Kraepelin was always in some doubt about his classification of this form of mental disorder. Yet he felt he was probably justified in regarding it as a manifestation of schizophrenia.

On this subject Henderson and Gillespie recently altered their views and now group such paranoid states not with the schizophrenic reaction type but with the paranoic and paranoid reaction type, thus altering the classification of schizophrenic states or dementia præcox as formulated by Kraepelin. They believe that the crux of the situation from the standpoint of differential diagnosis is determined by the underlying type of personality.

It is of interest to note that White (1936), from an examination of similar material was likewise disposed to separate all paranoid states from the schizophrenic group.

The differentiation of manic-depressive and involutional depressive states, from the schizophrenic and paranoid psychoses, is not infrequently a matter of great difficulty, although in a general way Kraepelin's broad division continues to be of considerable practical value.

Recently the idea has been revived of amalgamating the schizophrenic and the affective psychoses, using the term schizo-affective states, in the belief that they constitute the extremes of a continuous series of variables (Cobb, 1941). Penrose (1946) too, as a result of his statistical investigations has doubted the justification of clear differentiation among the affective, schizophrenic and paranoid reactive types.

The difference of opinion in regard to the best terminology to use tends further to complicate the issue. Thus Darrah (1940) suggests that the term, dementia præcox be used for a group of cases of insidious onset and bad prognosis, and that schizophrenia be reserved for acute cases of more favourable prognosis. Osborne (1940) favours the replacement of both dementia præcox and schizophrenia with the term palæophrenia, since mental testing

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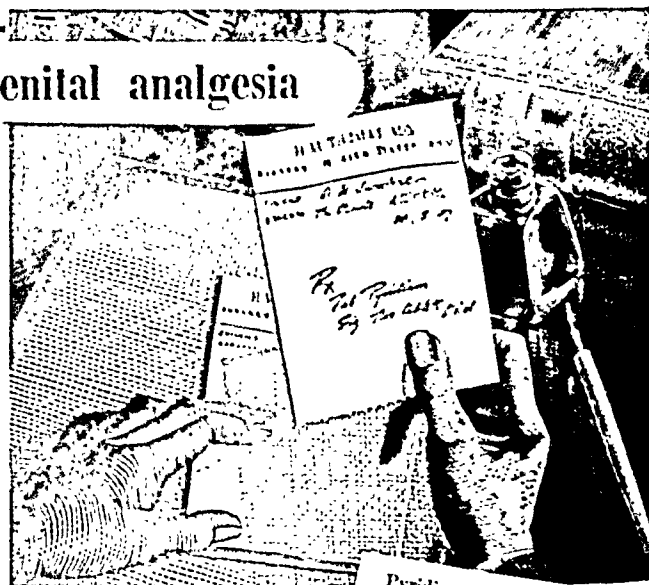
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in such states shows an impairment of conceptive thinking of a regressive nature.

**DEFINITIONS.**—It can be clearly seen therefore that the subject of classification in psychiatry has proved a difficult one and that, although a certain measure of agreement has been reached, not even in regard to broad groupings is opinion unanimous.

The difficulties of accurate classification and early diagnosis in psychiatry must be freely admitted.

I am acutely aware of the frequent overlapping in the manifestations of psychiatric syndromes which makes attempts at precise grouping even undesirable in the present state of our knowledge.

It is possible, however, that the symptoms and outcome have received unwarranted emphasis in the formulation of classification systems and that a more rational and useful subdivision of cases can be derived from the study of mental illness in relation to the personality development and the details of experience. This involves a review of constitutional, historical and situational factors and the dynamics involved in their complex inter-relationship. By so doing, general patterns of reaction can be found which materially aid the grouping of cases.

Such an approach allows of a separation of Schizophrenic and Paranoid Reaction Types.

Before considering to which of these categories the so-called paranoid schizophrenia is more closely allied, and to clarify my conception of these two broad groups, a brief description of them seems necessary.

The number of theories suggesting their ætiology makes clear the inadequate knowledge which exists in this direction. The constitutional, the psychological, and the organic approaches have all their followers. More recently, complex investigation of metabolism and autonomic function have raised fresh hopes of a clearer understanding. Nevertheless, if specific agencies are involved they have so far eluded research and many prefer to steer a middle course, accepting the part responsibility of all the above-mentioned factors. The theory of multiple causation which emphasises the importance of the personality structure and the total experience seems at the same time the most rational approach and that most likely to provide a practical basis for the differentiation of these states within the limits of our present knowledge.

A schizophrenic reaction type is one or other of a series of psychotic conditions which have as their common characteristic a destruction of the inner connections of the mind of a peculiar kind. This shows itself predominantly in a weakening of the emotional response and in an incongruity of affect, volition and thought. Interest is increasingly withdrawn from reality, and preoccupied with phantasy. Mental deterioration proceeds slowly but steadily to a terminal state which ultimately develops from varying initial clinical features. The course



may be interrupted by remissions of varying duration and degree. It may be that some recover, although the yardstick by which this is measured is difficult to standardise. It is customary to describe the simple, the hebephrenic, the catatonic and the paranoid forms of this process. In the first there is a slow, insidious and almost imperceptible disintegration of the whole psychic life. The hebephrenic exhibits characteristically profound personality devastation, a gross incoherence of thought, mood and behaviour, episodes of wild excitement, delusions and prominent hallucinations. The catatonic is differentiated by a tendency to exhibit alternating reactions of stupor and excitement on a background of schizophrenic symptoms. The paranoid form has already been briefly described. The majority of schizophrenic reaction types ultimately proceed to an end stage of considerable mental enfeeblement.

Regarding the associated personality type, it seems that most pre-disposed are those who have from an early age presented neurotic symptoms—excessive shyness, backwardness, lack of ambition, idiosyncracies, perversities, and oddities of behaviour, and who during their lives have lacked the ability to adapt themselves to society and to undertake any satisfying and useful activity with increasing feelings of inadequacy and insecurity. Such persons may slowly and insidiously in the course of months or years develop the abnormal reactions to life which are termed schizophrenic.

A paranoid reaction type is one or other of a series of psychotic conditions which occur predominately during the third decade of life. Delusions of persecution, which may later be followed by those of a more grandiose nature are outstanding. Hallucinations may or may not be present. The fixity of the delusions vary from those that are unchangeable and gradually elaborated by a process of logical reasoning into a coherent system, to those that are fleeting, inconstant, and poorly systematised. The illness is insidious in its onset. The personality becomes transformed as a result of misinterpretation and impairment of discrimination and judgment. Personality deterioration and affective impoverishment are not prominent. Complete personality devastation is characteristically absent. It is usual to describe two forms of the paranoid reaction type—paranoia and paraphrenia. The first is a chronic, systematised delusional state of unfavourable prognosis characterised by the fundamental unchangeableness of the delusions and the absence of hallucinations. In pure form it is uncommon. The second is differentiated by the less well-systematised and variable delusions and by the presence of hallucinations.

The associated personality type is one that may have shown little deviation from the normal. Not infrequently the school and work records are entirely satisfactory. In their respective walks of life many have performed their duties diligently and conscientiously, with the attainment of considerable success. Many are, however, touchy, ill-adaptive, hypersensitive, and suspicious-minded. There are frequent

indications of overweening pride and ambition. They are those who tend to be over-anxious, irritable and continually on the defensive in their social relations. They tend to misinterpret innocent circumstances and they are easily dominated by over-determined ideas ill-founded in fact. The stage thus set, it is but a short step to the formation of paranoid delusions.

In addition to these reaction types, two further syndromes require mention. Psychoses are not uncommon in which schizophrenic symptoms are prominent. I am of the opinion that in a great majority of these the schizophrenic manifestations merely colour a clinical picture which is primarily determined by some other cause, *e.g.* a toxic-exhaustive psychosis. Diagnosis, management and prognosis in these cases should be based more on the underlying cause than on the schizophrenic symptoms.

Frequently encountered also is a psychosis which has been termed abortive paranoia. It is a transient, delusional state with or without hallucinations and with a content which is often self-accusatory. The prognosis is good and its possible alliance to the manic-depressive psychosis has been suggested.

### GENERAL DISCUSSION

In examining and re-assessing the clinical material, study was directed in the first place to the personality development and structure, and the details of the life experience. The evolution of symptoms and the course of the disorder were then reviewed. Finally, a relationship was sought between the constitutional, historical and situational factors on the one hand, and the symptoms and course on the other.

In seven there was a positive family history of nervous or mental illness, as would be expected since 50-60 per cent. of such material shows a family record of mental breakdown. The nature of these family reactions here were predominantly depressive with four instances of suicide. The association of paranoid and depressive states is not uncommon. Gaupp (quoted by Kraepelin) mentioned cases with what he called depressive-paranoid disposition in whom, under the pressure of painful circumstances, a distrustful delusion of reference with a certain amount of insight and fluctuating course insidiously developed without leading to rigid systematisation. Schulz (1940) in his investigations on heredity believes it possible that there is a genetic factor common to both manic-depressives and schizophrenics (using schizophrenia in its widest sense). The work of Cobb and Penrose in this regard has already been mentioned.

In the early family situations there were four cases of disrupted home life and deficient parental example due to the early death or departure of one or other parent, and an equivalent situation as a result of illegitimacy, in two further cases. In all but one, the family situation in early life was described as unsatisfactory due to such

factors as alcoholism, parental disharmony, mental illness, suicide, broken homes and illegitimacy. It is here of interest to note that Faris and Dunham (1939) in an investigation of the social incidence of schizophrenia found the pattern of distribution was similar to that of many social abnormalities, and that the paranoid states followed this pattern most closely. This would seem to confirm the importance of a study of the life experience for a proper understanding of these reactions.

In half the cases there was little to suggest nervous traits in childhood and adolescence. In the remainder, these were present in the form of stammering, feeling of nervous tension and various fears.

The satisfactory school and work records in the great majority of cases seem to indicate a degree of maturity and personality integration which surpasses that usually found in the potential schizophrenic, and yet in certain aspects of social adaptation, deviations of response demonstrate defects of personality structure. Thus, in the seven married cases, six gave evidence of marital disharmony. The possible association of this with latent homosexuality seems likely. In six cases there was a suggestion of such trends in the pre-psychotic state, and in three of these this was strengthened by the appearance later of homosexual delusions. The importance of this factor in the genesis of paranoia is stressed by the psychoanalytic school (Freud, 1925).

In regard to the psychotic development, the average age of onset was over thirty years. This is rather later than is usually found in the schizophrenic reaction type, where the maximum incidence is about the twenty-fifth year.

All the cases began with paranoid symptoms in the forefront and such symptoms have continued to dominate the clinical pictures throughout their course. Half the cases showed an admixture of depressive symptoms with four instances of suicidal attempts. Further, it should be noted that five of them showed some degree of periodicity in the manifestations of gross symptoms, which allowed of temporary social adjustment. In the course of development the delusions, which were at first to some extent systematised, became poorly systematised, or unsystematised. Expansive ideas appeared in five cases. In eleven the delusions became of a bizarre and fantastic nature, and a similar number showed hallucinations. The emotional reaction was impaired in eight cases; in five of these this was not a prominent feature and was apparent only from time to time as a response, rather shallow, and less than the situation seemed to demand. This was associated with a similar degree of disharmony between mood, thought and behaviour. In three the effect was frequently inadequate, but in no case was there that persistent dullness, indifference, and apathy which characterises the schizophrenic state. Four showed a diffuseness in their talk from time to time, and in one this episodically amounted to disconnection. Gross incoherence, however, was characteristically absent. Three-quarters of the cases had no understanding of their

illness and in the remainder the insight was but partial. Yet, a terminal state with unmistakable symptoms of weakmindedness, which Kraepelin thought was usually reached in the majority of schizophrenic cases in the course of two or three years, was in no instance found in this material and, after an average duration of five years and more, the personalities were retained at a surprisingly good level.

Therefore, it is reasonable to suggest that these paranoid states are much more closely allied to the paranoid reaction type than to the schizophrenic reaction type, and that this alliance is apparent in the pre-psychotic personality, the symptoms and the course. It is true that some schizoid features appear in the personality and schizophrenic symptoms in the clinical picture. It is equally true, however, that schizophrenic symptoms may appear in other states; thus, they may be found in what is essentially a toxic-exhaustive psychosis, a manic-depressive, or psychopathic state, or they may constitute the prominent features of those suffering basically from some organic cerebral damage. With this in mind it is not unreasonable to believe that schizophrenic symptoms may appear in what is essentially a different process, namely, paranoid reaction type. This would seem to be borne out by the clinical findings. We do not speak in terms of toxic-exhaustive schizophrenia, or psychopathic schizophrenia for such clinical expressions would merely serve to complicate the issue and obscure the essential diagnosis. It seems unlikely, therefore, that we are any more justified in using the term "paranoid schizophrenia" for a state which is characterised and dominated by paranoid delusions and hallucinations which seems fundamentally determined by a paranoid make-up, which runs a chronic insidious course or one showing a certain periodicity, and in which the personality is well-retained after many years—even if schizophrenic symptoms may appear from time to time throughout the illness. Detachment from the external world, incongruity of feeling, incoherence of thought and peculiarities of behaviour—the cardinal symptoms of schizophrenia—nowhere dominate the clinical picture here. It seems in the sphere of discrimination, judgment and interpretation that the characteristic impairment is to be found.

The paranoid-depressive admixture already mentioned in this series, the tendency to some periodicity in the manifestation of gross symptoms, and the depressive family history require further consideration. A very large literature has arisen in regard to physical methods of treatment in psychiatry and more than a passing reference to it is beyond the scope of this paper. It is rather striking, however, that in the treatment of schizophrenia by electric convulsion therapy, insulin therapy and prefrontal leucotomy, probably the majority of investigators report the best results in the paranoid states. Thus, with electric convulsion therapy, Kalinowsky and Worthing (1943) consider paranoid schizophrenia with delusions and hallucinations to have the best outcome. In regard to the idea that insulin produces better results with paranoid schizophrenia than with any other types,

Henderson and Gillespie (1946), suggest that the material may be in fact episodic paranoid states bearing a close relationship to the manic-depressive group. In the treatment of schizophrenia by prefrontal leucotomy, Frank (1946), obtained his best results with the paranoid states, and goes on to comment that the implication of clinical experiences with regard to prognosis in both insulin and leucotomy treatment of schizophrenics may necessitate again the splitting of such cases into dementia præcox and paranoid groups as separate disease entities contrary to Bleuler's views.

It has already been stated that White, and Henderson and Gillespie have felt disposed to separate all paranoid states from schizophrenia. This paper would seem to strengthen such a view, and what might be termed the therapeutic tests here mentioned constitute yet further confirmation. Such physical treatments are most effective where the prepsychotic personality is better integrated, and electric convulsion therapy and leucotomy have been of particular value in such affective states as involutional depressions. The case material here presented, together with the reported results of physical therapy, suggest that paranoid states may be more closely associated with affective disorders than has been generally realised.

The nature and the relationship of the schizophrenic and the paranoid states has received much consideration in the past. It has been suggested that such comprehensive terms as the "schizophrenic-paranoid series" or "paraphrenia" might be used in regard to them to emphasise their essential unity, in the belief that the difference is one of degree and not of kind. To so criticise their separation on this assumption seems to me irrational. In psychiatric practice it is the exception to find states in anything approaching pure form. Overlapping in greater or less degree of well-known syndromes is almost constant, nor, in many cases, is it possible to clearly separate neurosis from psychosis. Thus, viewing the subject broadly, the suggestion that we are dealing with differences of degree and not of kind could with equal justification have a much wider application. Should this argument be carried to its logical conclusion we would eventually return to the concept of one, and only one, mental disorder. Such an approach seems hardly destined to clarify the issue. Further, to speak in terms of kind is to assume a knowledge of ætiology which we do not possess.

I believe, therefore, that all paranoid states should be separated from schizophrenia and regrouped with paranoia and paraphrenia under the heading of the paranoid-reaction type, without attempting too fine a differentiation between these included sub-groups.

This division is based on the pre-psychotic personality type, the reactive tendencies, and the symptoms and course, which are found to have a pattern common to all. By so doing, I believe that the determination of the prognosis, and the outcome in deterioration can be facilitated, and that the probable response to the newer physical methods of treatment can be more accurately assessed.

## CONCLUSIONS

(1) Paranoid states are more closely allied to the paranoid reaction type than to the schizophrenic reaction type for the following reasons :—

- (a) The pre-psychotic personality is rather different from the schizoid type and approximates more closely to the paranoid make-up, with frequent appearance of latent homosexual trends.
- (b) The social adaptability, as indicated by the school and work record and general adjustment, indicates a degree of maturity and personality integration seldom found in pre-schizophrenic states.
- (c) The age of onset is usually later than in the schizophrenic reaction type.
- (d) The clinical picture is introduced by paranoid delusions which continue dominant throughout its course in contrast to the schizophrenic reaction type, where delusions are secondarily determined by affective delapidation.
- (e) There is little to indicate personality disintegration and mental deterioration after illnesses of several years, of the kind that is seen in the schizophrenic reaction type after illnesses of two or three years and often very much earlier.
- (f) A common constellation of reactive tendencies whose pattern is predominantly paranoid can be traced throughout the life histories and psychotic developments.

(2) Confirmation of the contention that paranoid states involve a different process from schizophrenia is obtained by a reference to the literature in regard to the newer physical methods of treatment in such conditions. There it is found that with insulin, electric convulsions, and prefrontal leucotomy the best results are claimed in the paranoid states.

(3) The association of paranoid and affective disorders is here demonstrated, and it is suggested that this association may be stronger than has been generally realised. This relationship may in part determine the more favourable response to physical therapy so frequently found in paranoid states.

I wish to thank Professor Sir David K. Henderson for permitting me to use the clinical material and case records at the Royal Edinburgh Hospital for Nervous and Mental Disorders for the purposes of this investigation and the Faculty of Medicine of the University of Edinburgh for allowing me to publish this abstract of my M.D. Thesis.

## APPENDIX

CASE NO. 1—L. R., aged 39.—The patient was an illegitimate child. His mother became insane five months after his birth and entered a mental hospital. A diagnosis of adolescent insanity was made. She was described as a healthy, well-built Orcadian woman who was dull, confused, and unresponsive although quiet and manageable. While in the ward she used to sit with hanging head, apparently withdrawn from her environment. After

occasions with negative results. He is a man of average size and good general physique.

After an illness of twelve years' duration this patient continues to have delusions of reference and persecution. He adopts an attitude of superiority to others and, for the most part, remains aloof. He is suggestible and frequently, in the course of conversation, a smile plays around his lips in a facile way, suggesting a degree of independence of thought and mood. His behaviour is correct; he is an excellent gardener and undertakes skilled jobs without supervision. He has certain privileges which he has never abused. About his personal appearance he is particular, and is always well-groomed. His talk shows little that is abnormal, and when confidence is established he relates his past and present difficulties. Yet, an attitude of suspicion prevails and becomes more pronounced in the company of strangers, so that it is with difficulty that information can be elicited from him. The occasional impression of facility gained from his facial expression and his disinclination to speak suggest to those less well-acquainted with him a state of apathy and indifference, which is not borne out by more careful scrutiny. The slight affective blunting and incongruity have been noted, but, for the most part, the personality is well integrated and there is little to suggest mental decline. The emotionless, apathetic, deteriorated picture so frequent in schizophrenia of long standing is here conspicuously absent.

The clinical picture was ushered in at the age of twenty-eight years with paranoid symptoms. Initially, there was a strong depressive component. The striking feature is the well-retained personality after the lapse of twelve years. An examination of the personality structure, and the details of experience reveal significant material. The patient was illegitimate. Five months after his birth his mother became mentally involved and committed suicide in a mental hospital some months later. There was thus separation from the mother in early life and there was no father. He was a quiet, reserved, and conscientious child and later became an efficient and industrious workman. Paranoid traits came to dominate his personality in which there were also strong obsessional trends and a tendency to affective lability. During the first eighteen months of his illness the disorder of mood was prominent, and both depressive and manic phases appeared. Thereafter, the paranoid symptoms continued to dominate the clinical picture throughout its course.

To write in terms of psychopathology is, at best, to speculate reasonably of cause and effect. The family history may indicate predisposition. The knowledge of illegitimacy and the absence of parental example may have produced feelings of inferiority and inadequacy mirrored in childhood reserve. The adult paranoid-obsessive personality may be in part determined by the basic genetic equipment and in part compensation for feelings of humbleness and insecurity, derived from the constitution and early environment. With such a sensitive, conceited, jealous and obsessional character—ever ready to misinterpret, insinuate, and accuse, the scene is set for further and more grave developments. Marital disharmony was the first indication of difficulty in social adaptation. The marriage was not wholly of choice, the first child being born six months later. Under other circumstances he might have remained single. The jealousy and suspicion seem projections of his own failings. Psychoanalysts have stressed the strong homosexual component of the paranoid make-up. The miserliness and meticulousness further indicate abnormal trends. There developed an emotional indifference towards his

wife. Such hetero-sexual maladjustment may have produced further regression to the homosexual level which was inadequately repressed and resulted in projection, so maintaining the internal equilibrium at the price of psychotic development. The nature of the persecutory delusions—that the patient was having intercourse with other men—would seem to confirm these speculations. About the same time as the delusive developments there was an alteration of mood, with tension, agitation, depression and ideas of unworthiness. The prominent affective disorder in the early stages exemplifies what was stressed by earlier writers and the association of affective and paranoid symptoms has been already mentioned.

Thus, it may be that faced with an intolerable life situation such a personality reacted by misinterpreting reality. The personality was such, however, that its cohesiveness and the stability of its integration disallowed of a total collapse and retreat, so that after twelve years of mental illness it remains well-retained.

CASE NO. 2—J. T. R., aged 37.—The mother was a chronic alcoholic, and suffered from diabetes mellitus. No other history of nervous or mental illness in the family was given. The father was an engine-driver who died at the age of fifty. The patient was the youngest of a family of four. He was born in South Africa, and no abnormal traits were reported in infancy and childhood. It was, however, stressed that the family situation was unsatisfactory on account of the mother's alcoholism. He was an average scholar and attended school from five to fourteen years. On leaving school he became employed in a wine merchant's office, where he stayed for a year. He left, alleging that his mother's drinking bouts were bringing disgrace upon him. He next became an apprentice engineer, but he was sensitive and rather aggressive, and found it difficult to adapt himself, so that there were frequent "misunderstandings with other men."

It was not possible to obtain confirmation of the events which immediately followed, but it seems that the patient's sisters, having inherited some money, thought it an opportune moment to rid themselves of the alcoholic parent. They therefore suggested that she should go to friends in Britain, and it was arranged that the patient should accompany her and there complete his apprenticeship. The sisters promised that they would thereafter pay his passage back to South Africa. The patient and his mother duly arrived in Glasgow, where the former served his apprenticeship. Difficulties, however, arose in regard to the return passage, and the patient concluded his family did not want him.

In 1921 he married, and entered an oil business; this failed in 1923. He was idle for a time, and then came to Edinburgh, where he obtained work but stayed only for a few months. He got another job with a firm of engineers but, after some months, developed "severe colitis," and was in hospital for three months. On his return, he found the work too heavy and resigned. For the next few years he moved from job to job, staying but a short time in each, although being fairly regularly employed.

From 1931 till 1937, however, he was only sporadically employed. Two years after the marriage a daughter was born. There were no other children. The marriage was not a happy one; the patient was moody, tended to brood, and to be discontented, showed jealous traits and was given to outbursts of bad temper, so that there were frequent rows and disagreements.

In 1937 he was asked to take a six months' training course in engineering



and indifference was ever seen. Mannerisms, stereotypes, and other behaviour anomalies were absent, except for outbursts of assaultive behaviour determined by persecutory delusions and hallucinations. After nine years the personality was well-retained and mental deterioration was not a noticeable feature.

The mother was unstable and a chronic alcoholic. The patient was the youngest of four. Parental disharmony and alcoholism resulted in an unhappy early home situation. In the course of the personality development the following traits became clear—sensitiveness and feelings of inferiority, aggressiveness, and an inability to adapt socially. This resulted in frequent "misunderstandings with others." To these were later added more conspicuous paranoid trends; thus, his suspicions led to the development of over-determined and illogical notions—that he was not wanted; that he was the "odd man out"; that he was denied the opportunities given to others; that he was being passed over and ignored. He became querulent and demanded redress. When it was proved that he was acting unreasonably, he remained unconvinced. Delusions of persecution followed, with latterly transient appearance of depression with suicidal attempt. Gradually, there evolved poorly-systematised bizarre delusions, with hallucinations, and aggressive and anti-social behaviour.

Here can be clearly seen the state of affairs which Meyer (1906) described as a transformation of the personality in which reason is preserved but side-tracked; where the individual is continually ready to see a biased meaning in things, and where to the indifferent actions of others are attributed deliberate intentions, where suspicion and an anti-social attitude prevail.

Constitutional predisposition may be here present as a legacy from the unstable, alcoholic mother. The early unsatisfactory environment may have sown seeds of difficulties to come. The jealousy and suspicion; the marital disharmony, and the tactile genital hallucinations substantiating delusions of assault may permit speculations of a latent homosexual trend. Feelings of inferiority and insecurity may derive from the constitution, or from it and the early family situation. Against such a background the needs of social adaptation were met by a further and more grave development of those very traits which characterised the personality. Thus, the paranoid pattern of reaction progressed to delusional formation and a perverted picture of reality was painted to compensate for personality deficiency. The strong affective undercurrent in such paranoid states has many times been stressed. White (1936) considers the intellectual aspects to be explanatory of the feelings—rationalisations of the position the patient finds himself in as interpreted by his feelings. Here the disorder of mood is again clear. The feelings of unworthiness, of being a burden to others; the agitation, and the determined suicidal attempt constituted a real, though short-lived, episode. May it be that temporarily the mechanism of projection and the ability to falsely rationalise the feelings were in abeyance, and allowed a glimpse into the turmoil of guilt and inferiority to be quickly closed from view by the further operation of these mechanisms which restore the internal equilibrium at the price of paranoid delusional development.

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## NEW BOOKS

*The Selected Writings of Benjamin Rush.* Edited by DAGOBERT D. RUNES. New York. 1947. Price 5 dols.

Among the many Americans who studied medicine at Edinburgh during the eighteenth century, none holds a more honoured place than Benjamin Rush (1745-813), the "American Sydenham," as he has been called. Shortly after his return to Philadelphia after taking his M.D. degree at Edinburgh, he was called to take part in fighting a severe epidemic of yellow fever which swept the city and caused many deaths. His conduct under this ordeal won for him high praise. Yet such fortitude was only part of his attitude towards all the many difficulties of his life. Benjamin Rush was one of the most eminent and influential men of his time, alike in medical practice and in the wider field of politics. All that he wrote, and his writings are numerous, is worthy of our attention even to-day. He championed many a worthy cause: the humane treatment of prisoners, the removal of the death penalty, the abolition of slavery, and cessation of the British oppression in colonial America. The present selection of his papers is well chosen and suitably classified. There is one group "On Good Government," another "On Education," and a third which, to the medical reader, is most interesting of all, "On Natural and Medical Sciences." Although Benjamin Rush lived at a time when medicine was still groping in the dark, and when the bacterial cause of disease was still unknown, his remarks on the existing conditions of practice betoken a vision and foresight truly remarkable. Each reader may choose for himself in the varied fare offered by those essays. The reviewer would accord a high place to the admirable lecture entitled "Observations and Reasoning in Medicine," and to the discourse "On Manners," a commentary on a tour of France in 1769. Other readers, more politically inclined, may prefer Rush's advocacy of a Peace Office for the United States, in place of a War Office, or his plan for a Federal University.

There is a satisfactory index, and a bibliography to guide the reader who may be tempted to pursue still further his quest of the versatile Benjamin Rush.

*The Head, Neck and Trunk. Muscles and Motor Points.* By DANIEL P. QUIRING. Pp. 115, with 103 illustrations. London: Henry Kimpton. 1947. Price 14s. net.

This volume is the companion to "The Extremities." It provides a most excellent demonstration of muscles. Indeed it could hardly do otherwise since each muscle is allocated a whole page in the book. Each page contains a beautiful drawing of the particular muscle and in addition its nerve and blood supply. Its origin and insertion are described also and reference given for two popular anatomical textbooks. It should prove a great help especially in the understanding of the smaller muscles, e.g. those of the larynx, which are not illustrated well in the textbooks as a rule.

*Forensic Medicine.* By KEITH SIMPSON, M.D. Pp. viii+335, with 114 illustrations. London: Edward Arnold & Co. 1947. Price 16s. net.

Dr Simpson, who lectures on this subject at Guy's Hospital, has aimed at producing a short textbook acceptable to the overworked medical student as a practical guide to this fascinating and important subject.

The book covers the usual branches of the subject and includes several chapters on various aspects of toxicology. It is well produced and excellently illustrated, but the textual descriptions might be regarded as somewhat condensed even for the undergraduate.

*Recent Advances in Public Health.* By J. L. BURN, M.D., D.H.Y., D.P.H. Pp. viii+409. Illustrated. London: J. & A. Churchill Ltd. 1947. Price 25s.

This book, which is excellently produced and illustrated, surveys *some* of the more important recent advances in the changing field of Public Health. The individual reader, according to his interests and experience, will question the degree of emphasis which Dr Burn has laid on certain aspects of the huge terrain here surveyed. That is not surprising in a work of this nature and does not detract from one's admiration of the masterful way in which the author has covered so much territory in such a concise manner. The text is considered in three main parts—Public Health and the Individual, Public Health and the Community, and Public Health and the Environment. It is sound practical public health brought up-to-date without any extravagant flights into social medicine.

The volume could be read with enjoyment and profit by any doctor and will be of especial interest to D.P.H. students and public health officials in general. The references are adequate and there are most helpful suggestions for further reading at the end of each chapter.

*The Rehabilitation of the Injured.* Volume 2. Remedial Gymnastics, by JOHN H. C. COLSON, M.C.S.P., M.A.O.T. Pp. xii+556, with 439 illustrations and figures. London: Cassell & Company Ltd. 1947. Price 30s. net.

The present volume, the second in this series, deals with the part played by remedial gymnastics in the rehabilitation programme.

The book is divided into seven parts. The earlier sections deal with the theory of remedial exercises, the uses of suspension apparatus, and cord and pulley and weight and pulley systems in assisted and resisted movements.

Part 5 is devoted to the treatment of the commoner bone and joint injuries. After a brief description of the types of injury in each region a progressive programme of exercises for the whole rehabilitation period is given.

The last two sections deal with the preparation of amputation stumps for artificial limbs and re-education in walking.

The book is thoroughly practical in its outlook and will be of value not only to the physiotherapist but also to medical men and others interested in rehabilitation work.

The many good photographs and diagrams assist the reader in following the descriptions in the text.

*Dying, Apparent Death and Resuscitation.* By S. JELLINEK, M.D. Pp. viii+263. London: Baillière, Tindal and Cox. 1947. Price 10s. 6d. net.

The author presents certain problems about which no work has yet appeared in medical literature. The subject of his book is the origin of the process of dying or thanatogenesis. Most of the author's material has been obtained from records of cases of sudden death due to electricity during the past forty-five years. The book presents a somewhat unusual subject in a most interesting manner.

*Brompton Hospital Reports.* Vol. XIV for 1945. Copies to be had from Brompton Hospital, London, S.W. 3. Price 10s. post free.

The present volume contains nine papers which have already appeared in various journals. There is a review of pulmonary tuberculosis by Maurice Davidson, an article on hydatid disease and one on the use of penicillin. Thoracic surgery is prominently represented by articles on pneumonectomy, chest injuries, œsophageal carcinoma and ligation of the patent ductus arteriosus. There are also papers on unusual thoracic tumours and on diaphragmatic hernia. All of these are up to the high standard which is expected from this famous institution.

With the present issue is printed an author index covering Volumes I to XIV and a subject index for the whole series.

## NEW EDITIONS

*Roentgen Interpretation.* By GEORGE W. HOLMES, M.D. and LAURENCE L. ROBBINS, M.D. Seventh Edition. Pp. 398, with 266 illustrations. London: Henry Kimpton. 1947. Price 35s. net.

In the production of the new edition of this well-known textbook on X-ray interpretation, Dr Laurence Robbins has replaced the late Dr Howard Ruggles as joint author.

Judged by modern standards some of the illustrations are disappointing, but in other respects there are few grounds for criticism and the book should continue to enjoy its well deserved popularity. Most radiological textbooks nowadays comprise several large volumes. For the many readers who seek a more modest presentation of the subject this smaller work can be confidently recommended.

*Experimental Physiology for Medical Students.* By D. T. HARRIS, M.D., D.Sc., F.INST.P. Fourth Edition. Pp. xi+299, with one colour plate and 257 illustrations. London: J. & A. Churchill Ltd. 1947. Price 18s.

The fourth edition of this book contains a considerable amount of new material, much of it concerned with the application of modern electrical devices to physiological problems. Many of the experiments described can hardly be carried out as routine in present-day crowded and cramped laboratories, and are more suited for senior physiology students than for second M.B. standard medical students.

At the same time the book fulfils a purpose which neither author or title suggest; in it are to be found brief accounts of most of the modern techniques in experimental and human physiology, often very well illustrated by diagrams, and as a work of reference or suggestion for workers in clinical physiology or experimental medicine there is no other comparable single source of such information.

*Internal Medicine in General Practice.* By ROBERT PRATT MCCOMBS, B.S., M.D., F.A.C.P. Second Edition. Pp. xv+741, with 122 illustrations. Philadelphia and London: W. B. Saunders Company. 1947. Price 42s.

As its title suggests this book is not an ordinary standard textbook, but has been planned to lay special emphasis on those diseases in which errors of diagnosis and therapy commonly occur. The importance of an orderly approach to the problem of diagnosis is stressed throughout.

The book is split up into sections on Disorders of the Heart, etc., and for each section there is an introduction, and then a consideration of diagnostic procedures and the significance of signs and symptoms. Special stress is laid on those methods which can be carried out in panel practice. The matter is completely up-to-date including chapters on the new antibiotics and allergic diseases.

This book, well written and produced, is easy to read and full of sound information, and can be most heartily recommended to all medical men.

*Health Facts for College Students.* By MAUDE LEE ETHEREDGE, M.D., D.P.H. Fifth Edition. Pp. xiv+439, with 75 figures. London: W. B. Saunders Company. 1947. Price 12s. 6d. net.

This book written for non-medical students, contains a great deal of information on anatomy, physiology and various diseases, as well as an account of personal and social hygiene. It is full of sound common sense and should be of the greatest value in disseminating information on the maintenance of good health.

*Symptoms and Signs in Clinical Medicine.* By E. NOBLE CHAMBERLAIN, M.D., N.S.C., F.R.C.P. Fourth Edition. Pp. 463, with 346 illustrations, 19 in colour. Bristol: John Wright & Sons Ltd. 1947. Price 30s. net.

In its new edition, this well-known book has undergone a number of minor changes, mainly in the chapters on the Examination of the Nervous System. The diagrams and photographs are of the usual high standard. It is unfortunate, however, that only the more gross clinical manifestations of disease lend themselves to photography. The colour drawing of the patient with obstructive jaundice, for instance, is not likely to add much to the student's knowledge.

The text is clearly written and physical signs are admirably related to diagnosis in a manner which will facilitate the student's understanding of the elements of clinical medicine. The book is a most useful adjunct to bedside teaching.

*Biology for Medical Students.* By C. C. HENTSCHEL and W. R. IVIMEY COOK. Fourth Edition. Pp. xii+752, with 453 illustrations. London: Longmans, Green and Co. 1947. Price 25s. net.

Textbooks are scarce these days, and this new edition will be welcomed on that account as well as because of its own particular merits. It deals with botany and zoology, and welds them loosely by a common chapter on cytology and later in an account of adaptation to environment. The botanical side, while dealing adequately with structure and reproduction, properly places strong emphasis on physiology, and interest as well as educational value have been added to the animal side by the inclusion, beyond the types usually studied and the accounts of histology and vertebrate embryology, of general chapters on environment and on various aspects of evolution and heredity.

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(John Wright & Sons Ltd., Bristol) 8s. 6d. per part
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# Edinburgh Medical Journal

August 1948

## ARTERIAL EMBOLISM

By J. R. LEARMONTH, C.B.E., Ch.M., F.R.C.S.E.

Regius Professor of Clinical Surgery and Professor of Surgery,  
University of Edinburgh

EMBOLI which provide clinical problems may be derived from any one of a number of sources, and in practice it is at least as important to identify the source of the embolus as it is to identify the artery which has been blocked, and the level at which the block has occurred. From the pathologist's point of view an arterial embolus may be derived :—

(1) From thrombi occupying the left auricle (auricular fibrillation) or left ventricle (coronary infarction) of the heart.

(2) From a thrombus accumulating on an atheromatous patch in a proximal segment of a vessel, from which the embolus is swept to lodge in a more distal and therefore narrower segment of the same vessel, or in one or more of its branches.

(3) From a detached portion of a thrombus which has formed in a vein : such an embolus may pass directly to the left side of the heart, through an opening in the interatrial septum, or it may form a pulmonary embolus which either by a process of distal thrombosis or by leading to localised pulmonary vascular stasis, produces a clot in a pulmonary vein which is carried thence to the heart.

(4) From the detachment of infected vegetations in bacterial endocarditis, and

(5) From the rapid dissemination of masses of tumour cells throughout the arterial system.

The surgeon, whose problem is immediate and practical, tends to divide arterial emboli into two simpler groups :—

(1) Those not open to direct surgical treatment—embolism of the visceral and cerebral arteries, and

(2) Those open to direct surgical treatment—aortic embolism and embolism of the peripheral arteries.

In most cases the clinical problem posed by the lodgement of an embolus does not differ from that posed by the sudden interruption of arterial flow in any other way—for example by division or ligature of the artery. The problem is “to secure a permanent adequate supply

A Honyman Gillespie Lecture delivered in the Royal Infirmary, Edinburgh, on 29th April 1948.



of arterial blood to tissues threatened with ischæmia, or already partly ischæmic." It will be convenient first to study this problem and to consider devices for assisting in its solution. In the order of their importance, the essential factors are :—

- (1) The preservation of adequate blood volume,
- (2) The maintenance of adequate general blood pressure, and
- (3) The adequacy of the collateral circulation.

In cases of arterial embolism, preservation of blood volume is never a factor and maintenance of adequate general blood pressure seldom, the exception being certain cases of coronary thrombosis; but the adequacy of collateral circulation is all-important, and must be examined further. The provision of adequate collateral circulation calls for ultimate structural alterations in the human body; and although nature is marvellously quick in making biophysical and biochemical adjustments, she requires time to complete structural adjustments. In cases of arterial embolism time is the one thing the clinician cannot afford to grant nature, because his period of usefulness is strictly limited to the critical survival period for each individual tissue after its blood supply ceases to be adequate, a period which varies from a minute or two for cerebral tissue to 24 hours or so for skin.

After the lodgement of an arterial embolus, the availability of collateral channels depends upon certain factors.

## 1. ANATOMICAL ARRANGEMENT

The number and calibre of collateral channels to bypass a block at any one site vary from individual to individual. Moreover there are certain levels in the courses of arteries, notorious for the lack of collateral vessels to bypass an interruption at these points: the axillary artery immediately beyond the origin of its subscapular branch, the common femoral artery, and the interruption of all three vessels at a point of bifurcation of any large artery: all have evil reputations, which I believe are not uniformly deserved. Certain collaterals may be at once available; they may be dissected easily, or demonstrated by arteriography. Others come into service at a later date, as a result of the enlargement of small vessels; contrary to orthodox teaching, muscular branches contribute little to this group. After arterial embolism the physiological function of collaterals is to bring blood back into the main arteries, not to provide a complete alternative pathway to them (Fig. 1).

## 2. PATHOLOGICAL CONDITIONS

Irrespective of their anatomical arrangement, the effectiveness of collateral channels may be reduced by the existence of pathological arterial states. Of these we must consider one disturbance of vascular physiology—arterial spasm; one disturbance of the clotting mechanism—consecutive thrombosis; and any structural change in the walls of arteries—usually of the nature of sclerosis.

(a) *Spasm*.—Spasm may reduce collateral supply in any or all of three ways: (1) by spasm of the collaterals themselves, (2) by spasm of the artery proximal to the embolus, reducing its calibre and that of the mouths of collaterals arising from it, and (3) by spasm of the artery distal to the embolus, producing a barrier to the return of blood through collaterals to the main trunk. The exact etiology of spasm is as incompletely understood as is its relief by therapeutic measures, but it may be a formidable complication of embolism. As I shall describe later, spasm of itself may be mistaken for embolism.

(b) *Consecutive Thrombosis*.—After the impaction of an embolus, thrombosis may proceed both proximally and distally in the arterial lumen; and this process may occlude the mouths of collaterals and so reduce their effectiveness. It is curious that collaterals whose orifices open into a thrombosed segment of artery may themselves remain patent, in spite of the sluggish current of blood within them, an observation made by Leriche (1937) (Fig. 2).

I have had one extraordinary example of the extent to which consecutive thrombosis may complicate embolism. The patient was an elderly woman, suffering from auricular fibrillation, admitted to my wards 48 hours after an

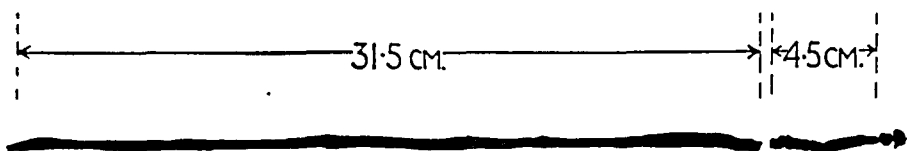


FIG. 3.—Thrombus withdrawn from femoral and popliteal arteries proximal to an embolus in the latter

episode which, from its history, indicated the lodgement of a popliteal embolus. The level of threatened gangrene indicated a higher block, and pulsation in the femoral artery was absent from a point a short distance below the inguinal ligament. In the belief that a second embolus had been impacted here, I exposed this segment first. I was able to withdraw, in one piece, a cast in thrombus of the femoral and popliteal arteries, and thereafter to remove the original embolus from the bifurcation of the popliteal artery (Fig. 3). I thought it possible that the sudden restoration of blood flow through partly ischaemic muscles might precipitate what we loosely call the "crush syndrome," but evidence of this did not appear. Eight days later the patient became unconscious and died. At autopsy cerebral arteriosclerosis was found.

(c) *Arteriosclerosis*.—It is obvious that organic changes in the walls of collateral vessels will not only narrow their lumina, either uniformly or patchily, but will also prevent their dilatation to carry greater volumes of blood. The possibility of natural recovery from the effects of lodgement of an arterial embolus thus becomes less as arteries lose their resilience with age.

From these considerations certain principles of what may be called the "first-aid treatment" of arterial embolism may be deduced, and I shall enumerate these before considering the various clinical types of arterial embolism, and their treatment.

(1) The patient should at once receive a dose of heparin, of 10,000 international units, to prevent consecutive thrombosis, and should remain under the influence of heparin until a decision is made for or against operation. If operation is required, the anticoagulant effect of heparin may be discontinued at once by the intravenous injection of protamine sulphate, which acts by discharging the large negative electric charge carried by the heparin molecules.

(2) To reduce metabolic demands, the threatened part should be put at rest, and maintained at a temperature of from 15° C. to 20° C.

(3) Pain should be suppressed, because it tends to irritate and to perpetuate arterial spasm.

(4) Sleep should be induced, because it promotes general vasodilatation.

(5) When auricular fibrillation is present, digitalis should be withheld unless there are signs of cardiac failure, in order to attempt to prevent the ejection of further clots from the left auricle.

## CLINICAL TYPES OF ARTERIAL EMBOLISM

### *A. Aortic Embolism*

I have operated for aortic embolism on four patients.

CASE 1.—A woman aged 36 had an operation for ruptured tubal pregnancy. On the 12th, 19th and 30th post-operative days she had pulmonary emboli, all affecting the left upper lobe. On the 32nd day she had an aortic embolus, associated with pain and loss of power in both legs, and anæsthesia to the groins. I saw the patient 11 hours later, and operated at once. I attempted to remove the embolus by suction through an incision in each common femoral artery, but was unable to do so. I then exposed the right common and external iliac arteries through Abernethy's extraperitoneal incision, but was still unable to milk down the clot. Finally I opened the peritoneum and broke up the clot by kneading the aortic bifurcation. When the aorta was cleared, and both arteriotomy wounds had been sutured, I had to make a second opening in the right superficial femoral artery, to recover a piece of embolus which had slipped past the controlling tape (Fig. 4). Heparin was given by continuous drip for 12 days (Fig. 5). To-day, two years after operation, the patient is living the busy life of a farmer's wife, and is expecting a baby soon.

CASE 2.—A woman, aged 42, known to suffer from auricular fibrillation, was admitted to Dr Rae Gilchrist's wards, nearly 24 hours after the lodgement of an aortic embolus, with early gangrene of both legs and anæsthesia and loss of power to mid-thigh. Although it was clear that her legs could not be preserved, Dr Gilchrist agreed that as she had a young child, an attempt should be made to preserve her life. The embolus was removed transperitoneally, through an incision in the right common iliac artery. The patient did not speak after operation, although she ate and drank, and 36 hours later she died. At autopsy thrombi were found in the left auricle, there were old infarcts in both kidneys, and recent infarcts in the spleen and in the distribution of both anterior cerebral arteries, in both of which emboli were found. Old organised emboli were present in the right external iliac and right common femoral arteries, and the patient must have been using collateral pathways to supply this limb, which was considerably less involved

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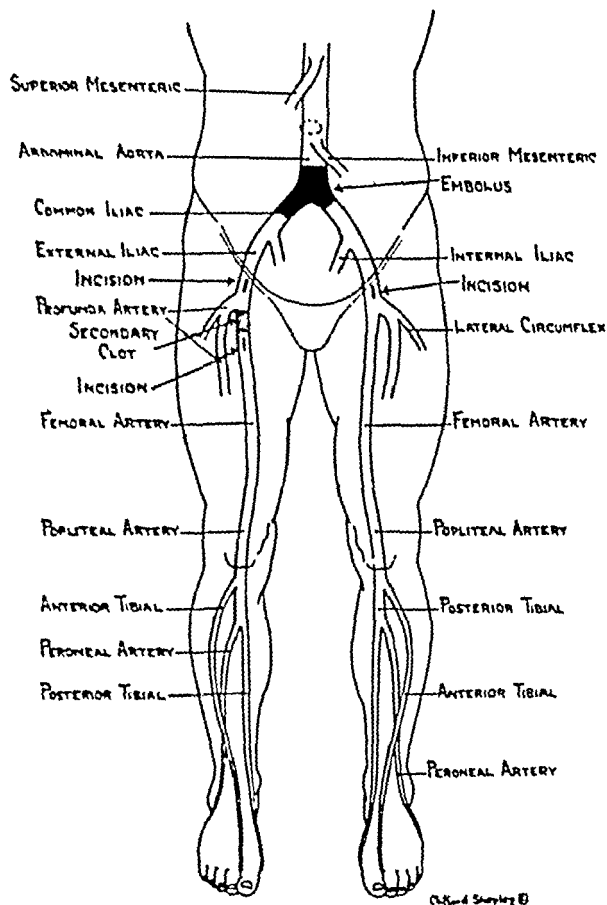


FIG. 4.—Case 1. Disposition of primary embolus and secondary clot, with sites of incision.

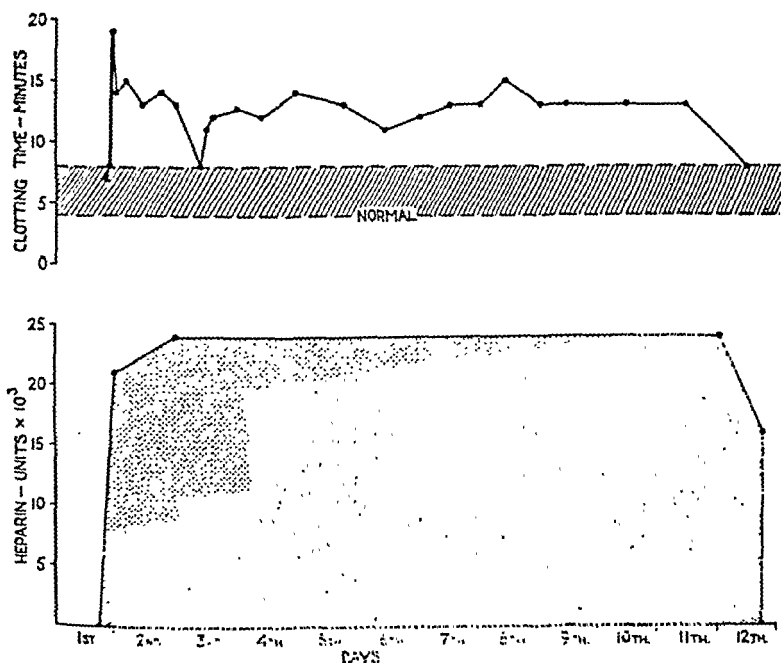


FIG. 5.—Case 1. Dosage of heparin, and clotting time, during post-operative period.

than the left (Fig. 6). This patient had both heparin and digitalis after operation. The arteriotomy wound was intact.

CASE 3.—A plethoric woman of 57 had had femoro-iliac venous thrombosis in the right leg, and a pulmonary embolus, following ligation of the right internal saphenous vein. Twenty-eight days after the ligation she had an aortic embolus, with sudden pain in the lumbar region, loss of power in both legs, and anæsthesia to the level of the 11th thoracic segment. Mr T. McW. Millar, whose patient she was, kindly asked me to deal with the condition,

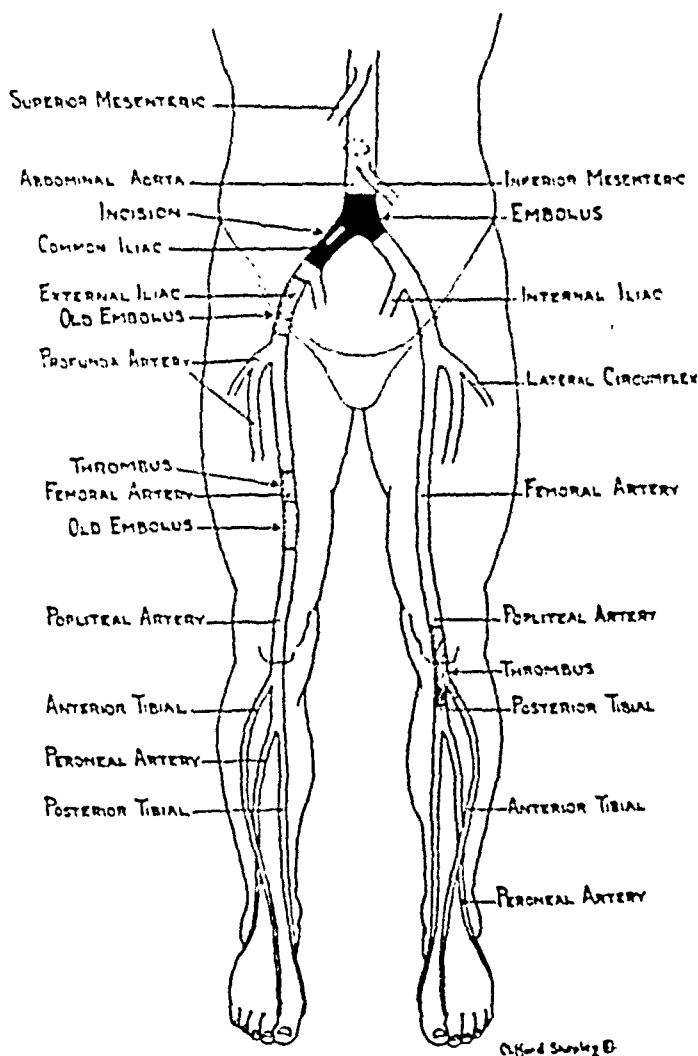


FIG. 6.—Case 2. Disposition of recent and old emboli and consecutive thrombi.

and three hours after its impaction I removed a very large embolus by the transperitoneal route, through an incision in the right common iliac artery. The next day she was only partly conscious and had a right facial palsy, and the nutrition of the left leg was impaired. For the first six days heparin was given by drip, and dicoumarol from the 5th to the 34th days (Fig. 7). Both the cerebral condition and the local condition of the legs rapidly improved. She had a long convalescence, complicated by a large sacral bed sore and by jaundice following a transfusion of plasma, but ultimately made a good recovery. Now, ten months after operation, she has slight weakness of the peronæi on the left side, and some patchy disturbance of sensation below the

left knee. This patient undoubtedly owes both her life and her legs to anticoagulant therapy under the constant attention of my colleague Dr Burt.

CASE 4.—A woman of 55, who had a long history of rheumatic endocarditis, was admitted to Dr W. D. D. Small's wards, shortly after an episode of coronary infarction. She was found to be fibrillating. Three weeks later she had sudden and quite painless loss of power in both legs, with anaesthesia to the level of the inguinal ligaments. Four hours later I removed the aortic embolus by the transperitoneal route and incision of the left common iliac artery. On the first post-operative day she had 21,000 units of heparin, which was then stopped. On the second, she had partial aphasia, which rapidly

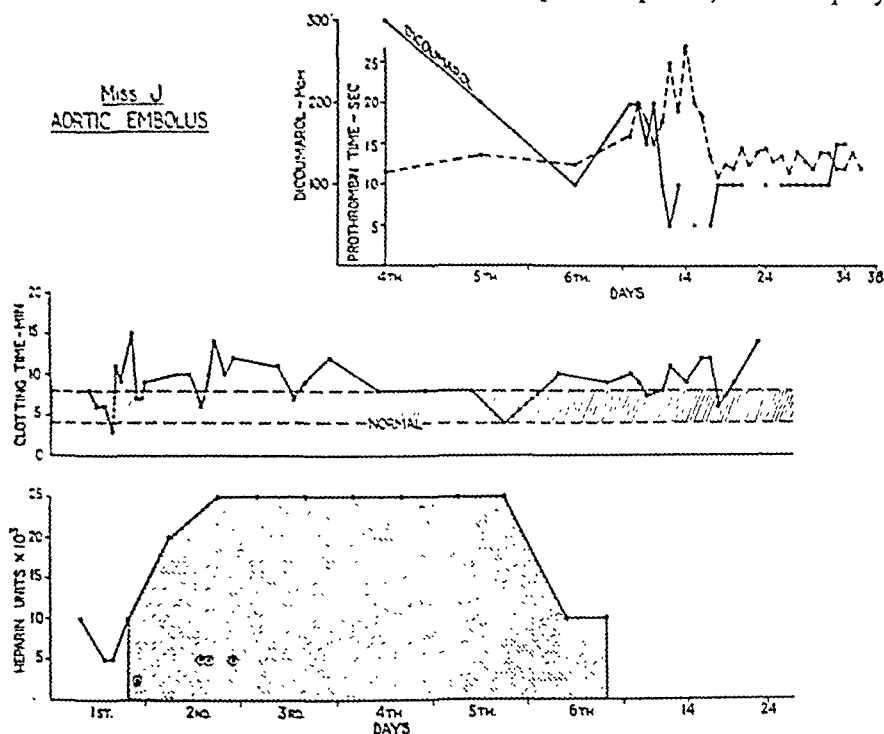


FIG. 7.—Case 3. Dosage of heparin and dicoumarol, with clotting time and prothrombin time, during post-operative period.

disappeared. On the 8th day (I am ashamed to confess) she had gross swelling of the left leg, as a result of femoro-iliac venous thrombosis, with clinical signs of a pulmonary embolus. Anticoagulant therapy was resumed (Fig. 8): for the first two days heparin alone was given; then dicoumarol was added. The heparin was discontinued on the 5th day, the dicoumarol on the 9th. From the 12th to the 14th day there was gross hæmaturia, for which large doses of vitamin K were administered. On the 15th day when the prothrombin time showed a late rise, she had a small cerebral embolus, with paralysis of the left side of the face, which took three days to disappear. Throughout the whole of this period, with the exception of the 3rd day, she was given digitalis. Ultimately she made a good immediate recovery, so far as her original cardiac condition permitted; but I was in error in failing to continue anticoagulant therapy after the first post-operative day. Five months after the aortic embolectomy, she was admitted to the medical unit in the Western General Hospital, with a large cerebral embolus causing complete left hemi-



plegia and conjugate deviation of the eyes to the right; in both legs the common femoral and posterior tibial pulses were present. At the limited autopsy the aortic bifurcation was secured; the aortic wall was smooth and a trifle blood-stained, the arteriotomy wound almost invisible (Fig. 9). The left common iliac vein was patent.

I believe that aortic emboli should be removed by the trans-peritoneal route, with arteriotomy of the common iliac artery on the side most involved: that post-operative anticoagulant therapy should be employed for seven to ten days, and that digitalis should be given if there are signs of cardiac failure.

Mas OD.    AORTIC EMBOLISM  
CEREBRAL EMBOLI 2 DAYS AND 23 DAYS POST OP.  
PULMONARY EMBOLISM: 8 DAYS POST OPERATIVE

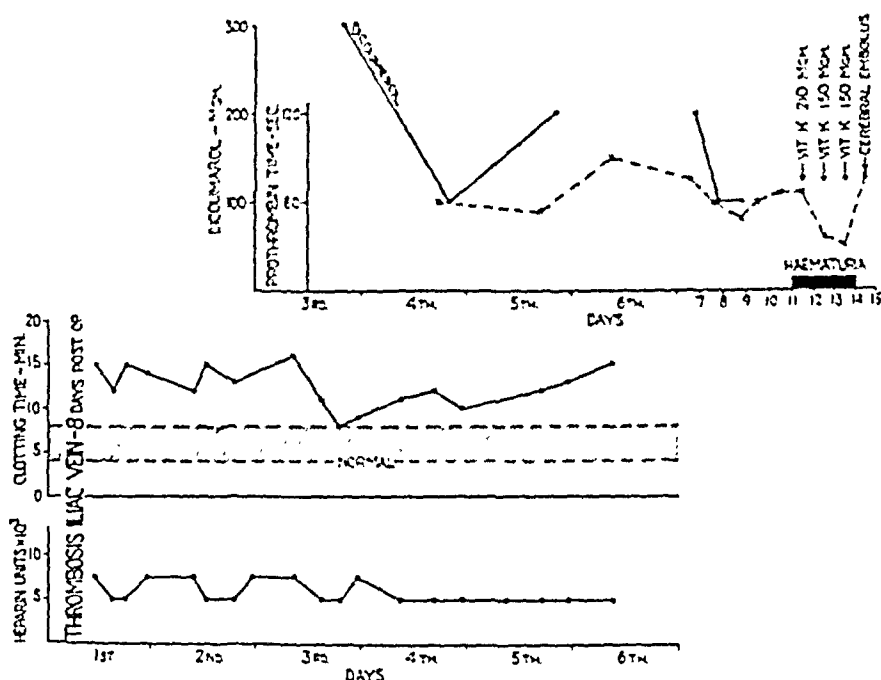


FIG. 8.—Case 4. Dosage of heparin and dicoumarol, with clotting time and prothrombin time, during post-operative period.

### B. *Peripheral Embolism*

The clinical features of embolism in a peripheral artery are pallor of the limb, absence of peripheral pulses, paralysis of motion and sensation, and usually, though not always, pain. To these local features must be added those of any cardiac disease present. When an embolus lodges in a peripheral vessel, the immediate treatment which I have described must be instituted at once: the measures are as available to the general practitioner as to the consultant in hospital. The ultimate treatment of the individual case depends upon a consideration of all the circumstances in that case; in the upper limb, and often in the lower limb, an initial policy of conservatism is best, especially when further emboli may be expected.



FIG. 1.—Arteriogram after ligation of the common femoral artery, showing refilling of the femoral artery through a lateral circumflex artery arising directly from the femoral proximal to the point of ligation.



FIG. 2.—Arteriogram in case of thromboangiitis obliterans, showing patent collateral (X) arising from thrombosed segment of popliteal artery.



FIG. 9.—Case 4. Posterior view of aorta and common iliac arteries, with posterior wall of left common iliac artery removed to show minimal scarring after arteriotomy.



FIG. 12.—Thrombus in posterior tibial artery of type readily detached.





FIG. 13.—Aorta and great vessels showing thrombus on atheromatous ulcer in left subclavian artery.

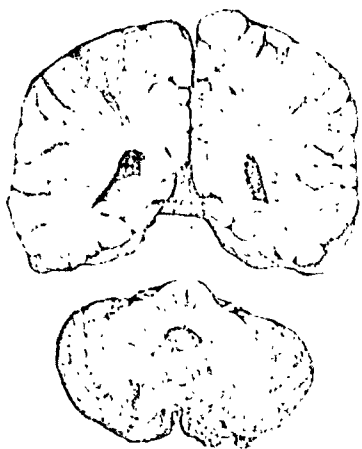


FIG. 14.—Sections through cerebrum and cerebellum showing old and recent infarcts.

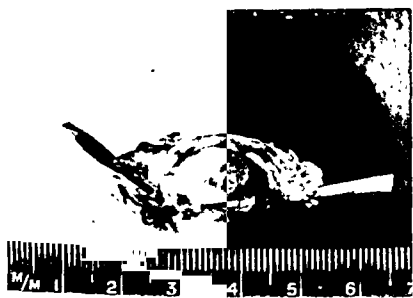


FIG. 15.—Bacterial aneurysm after excision.



FIG. 16.—Tumour embolus in branch of pulmonary artery ( $\times 140$ ).



Occasionally the course of clinical events settles the matter. Thus a patient, aged 73, who had mitral stenosis and auricular fibrillation, was admitted to my wards with impending gangrene of both feet. In spite of anticoagulant therapy, other emboli lodged in the vessels of the legs, and finally an embolus blocked the left renal artery (Fig. 10). At autopsy both recent and old emboli were found. In such cases surgery cannot help.

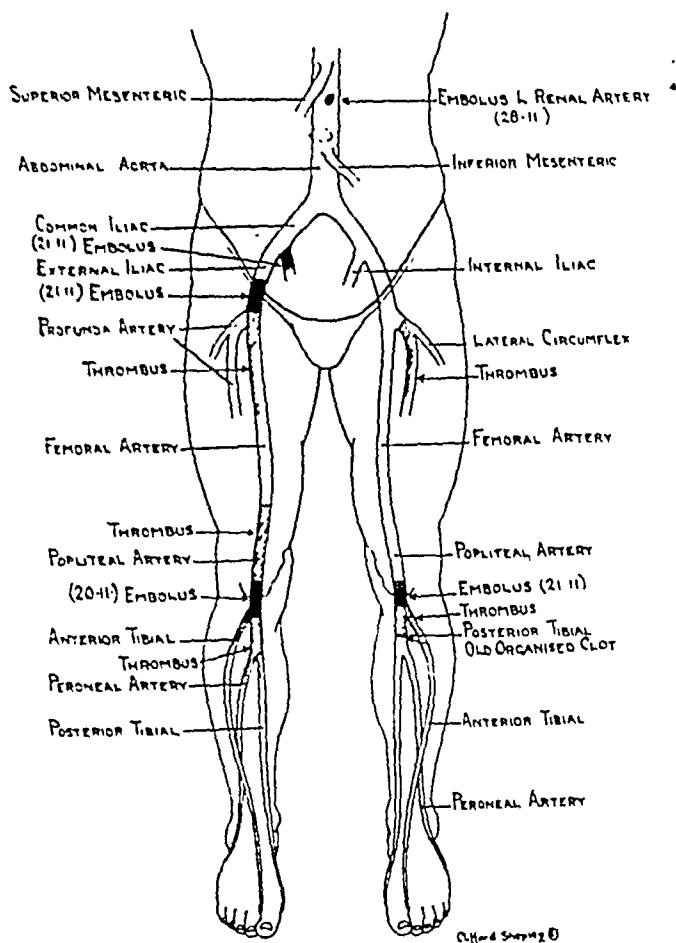


FIG. 10.—Disposition of multiple emboli and consecutive thrombi with dates of lodgement of emboli.

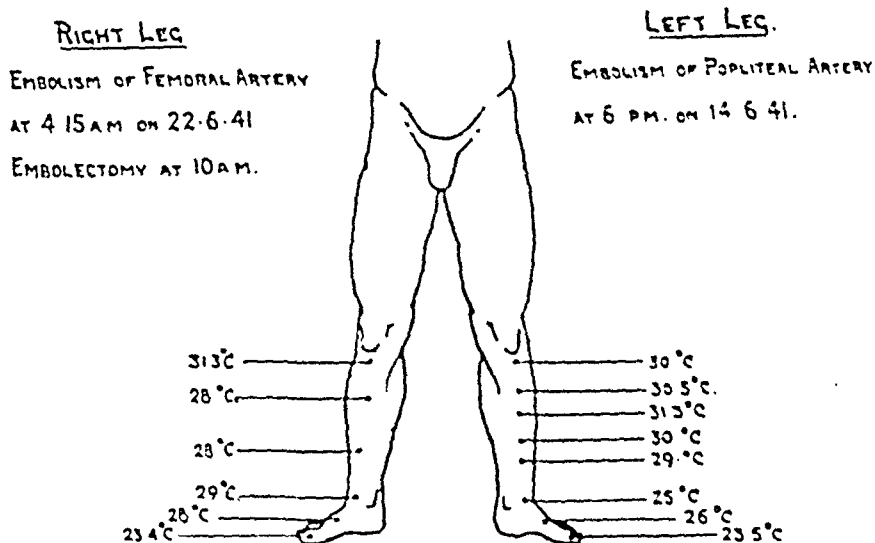
I have had an opportunity of comparing the results of conservative treatment of femoral embolism in one leg with the results of femoral embolectomy in the other.

A woman, aged 48, with auricular fibrillation, was admitted to Dr Rae Gilchrist's wards, with embolism of the left popliteal artery. As the embolus had lodged 18 hours previously, I advised against operation, and the patient was treated by reflex vasodilatation to encourage collateral flow; anti-coagulant drugs were not then available. Eight days later an embolus lodged in her right femoral artery, and was removed six hours later, under local anæsthesia. An hour after the operation had been finished, the cutaneous

temperatures of both legs showed little difference, although on the side of the embolectomy circulation had been restored at once (Fig. 11). Five days later the patient died from the lodgement of further multiple emboli.

Not infrequently patients are seen some time after the lodgement of an embolus (which may not have been recognised) who have made reasonable recoveries without any treatment. This may happen in either arm or leg, but is more likely in the arm, where the collateral circulation is better.

NAME. MISS. D. N...... AGE 48.... SEX ♀....  
 OCCUPATION. SEWING TEACHER..... DATE 22.6.41..  
 HOSPITAL DIAGNOSIS. EMBOLI..... CASE RECORD No 14, R.I.E.  
ORAL TEMPERATURE 98°F..... PULSE RATE 90....  
AV. ROOM TEMPERATURE 23°C. BLOOD PRESSURE 120/70 mm. Hg



NOTES. A VERY WARM SUMMER DAY READINGS MADE FROM 11-11.30 AM.  
ON 22.6.41, i.e. 1 HOUR AFTER EMBOLECTOMY.

FIG. 11.—Graph to show cutaneous temperatures following conservative treatment of embolus of left popliteal artery and surgical removal of embolus of right femoral.

A woman aged 77, who had auricular fibrillation, one morning felt a sudden pain in the right forearm, and forearm, hand and fingers became white. During the next 30 minutes the forearm and hand warmed up; later the fingers became warmer, but never quite so warm as on the unaffected side. Arm and hand tired readily. I saw her four days later. Both radial and ulnar pulses were absent; on elevation the hand and fingers became pale at once; in dependence, in the course of three or four minutes they became purple. The collateral circulation was just adequate for nutritional purposes, but could not as yet compete with gravity.

A woman of 54, known to have mitral stenosis, in March 1946 had severe pain, loss of power, coldness and discolouration of the right foot and leg. Gradually she recovered power in the leg, and nutritional lesions did not appear. I saw her seven months later, when the leg was bluish in colour and somewhat swollen, but she was managing to walk pretty well with the aid of a toespring. Popliteal, posterior tibial and dorsalis pedis pulses were absent, there was weakness of the anterior leg muscles, and anaesthesia of slipper distribution. My only therapeutic contribution was to substitute check-irons for the toespring, because the calf-strap securing the spring might have been constricting valuable collaterals running in the subcutaneous plane.

It is perhaps not sufficiently recognised that the lodgement of an embolus may be painless, even, as I have pointed out, in the aorta. Moreover, occasionally an embolus may lodge without the patient's knowledge, without any sign or symptom. I think it possible that some of these emboli—which may be discovered only at autopsy—are arrested during sleep, when all the arteries and arterioles are dilated. In my fatal case of aortic embolism, at autopsy old organised emboli were found in the right external iliac and right superficial femoral arteries, and the patient did not give any history of these episodes, nor could her relatives. Some painless though otherwise clinically recognisable cases of embolism may not be diagnosed at first, because of the absence of pain.

Thus a young woman, aged 21, who believed herself to be in excellent health, was sitting an examination in drawing when suddenly she lost the power of her right hand, the crayon falling from its grasp. The nature of the condition was not clear to the original observers, but some hours later Dr W. A. Alexander, with whom I saw the patient, found mitral stenosis to be present; the radial and ulnar pulses were absent, and the hand was still weak and cold. Within an hour or two the radial pulse returned and the hand rapidly became normal. No doubt the embolus had been thrust on from the bifurcation of the brachial artery into the ulnar artery. Obviously operation was not required.

An interesting group is that in which an embolus becomes detached from a mural thrombus in the wall of a large artery. The primary disease is usually atheroma, and it is likely that in the precarious limbs of *arteriosclerotics* massive gangrene is often precipitated in this way. I found such an example (Fig. 12) of a thrombus ripe for detachment in the posterior tibial artery of the amputated limb of a colleague, who had also a popliteal aneurysm. Emboli may also be derived from the sac of an aneurysm, to lodge in a peripheral vessel. Another source of emboli is the subclavian artery riding over a cervical rib, from the irritated wall of which small emboli may be detached to block digital arterioles and so to give rise to an acute Raynaud phenomenon. One or two examples will suffice.

A woman of 73 had an attack of numbness in the left hand, which soon disappeared. Later in the day numbness and coldness reappeared, but wore off in an hour, and she went to bed. In the morning she was awakened by agonising pain in the forearm, and found that the forearm and hand were



powerless. There was some delay in her admission to the Western General Hospital under the care of Mr John Bruce, when the arm was found to be anæsthetic to a point 2.5 cm. above the elbow. Two days later, as the arm was gangrenous, a rapid amputation was performed, but the general condition of the patient deteriorated and she died of broncho-pneumonia on the 15th day after the lodgement of the embolus. At autopsy a likely source for the embolus was found in a thrombus on a patch of atheroma in the left subclavian artery (Fig. 13).

A charwoman of 53 who had not had much previous trouble with her fingers, found one morning while at work that her right forefinger became, quite suddenly, white and painful. She was sent to my unit, where she was at once given heparin until dicoumarol could produce its effect. The pain rapidly disappeared, and there was no gross shrinking of the pulp of the finger. Twenty days later I removed the well-marked cervical rib, over which was riding a dilated subclavian artery. In such cases it is most important to prevent consecutive proximal thrombosis, by immediate anticoagulant therapy.

The strangest example of these emboli of arterial origin which I have encountered was that of a young naval rating who had a large traumatic aneurysm of the left common carotid artery, the result of a bomb wound. Progressive attacks of dyspnœa made operation imperative and five weeks after the wounding I ligated the left common carotid both at its origin from the aorta and distal to the sac of the aneurysm. The operation was without incident and the patient's immediate post-operative condition excellent; but eight hours after operation he died suddenly. At autopsy a cause for this sudden death could not be found in the thoracic cavity. When the brain was examined, old and recent infarcts were found in the left cerebral hemisphere, the result of detachment of emboli from the sac. But there were also infarcts of the left cerebellar hemisphere, and of the medulla, the latter being the cause of death (Fig. 14). This directed attention to the vertebral artery which was embedded in the postero-inferior wall of the sac, and the sequence of events became obvious.

Occasionally the end-results of the lodgement of bacterial emboli call for surgical intervention. When such an embolus is arrested in one of the vasa vasorum of a large artery, an abscess forms in the wall of the artery, which so weakens it that a bacterial aneurysm forms.

A young woman whom Dr Rae Gilchrist was treating for subacute bacterial endocarditis, developed a bacterial aneurysm in the distal part of the left popliteal artery. I excised this, including the origins of the anterior and posterior tibial arteries (Fig. 15). Three months later the posterior tibial pulse on the affected side had returned, and the skin temperatures were equal on both sides. A year later she died elsewhere, of a recrudescence of the primary disease.

Rarely in the terminal stages of malignant disease widespread dissemination of tumour cells occurs, in the form of arterial emboli. When such emboli block the finer vessels of the skin, multiple cutaneous infarcts result.

A man of 47 suffering from bronchogenic carcinoma underwent pneumonectomy at the hands of my colleague Mr Andrew Logan. Three months later

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numerous discrete infarcted patches appeared on the skin of both legs, and shortly afterwards he died with widespread metastases, including tumour emboli in the remaining pulmonary artery (Fig. 16).

Although the diagnosis is not often in doubt in cases of peripheral arterial embolism, there is one condition not unknown to cardiologists, in which all the features of embolism are present, except the embolus. The explanation usually given is that a segment of a main artery has gone into intense spasm, though why that should occur has not been explained. I have seen two cases of this type.

A woman aged 55, had had mitral stenosis and auricular fibrillation for five years, and during this period an embolus had lodged in the left brachial artery. Ten hours before admission to my wards, apparently an embolus

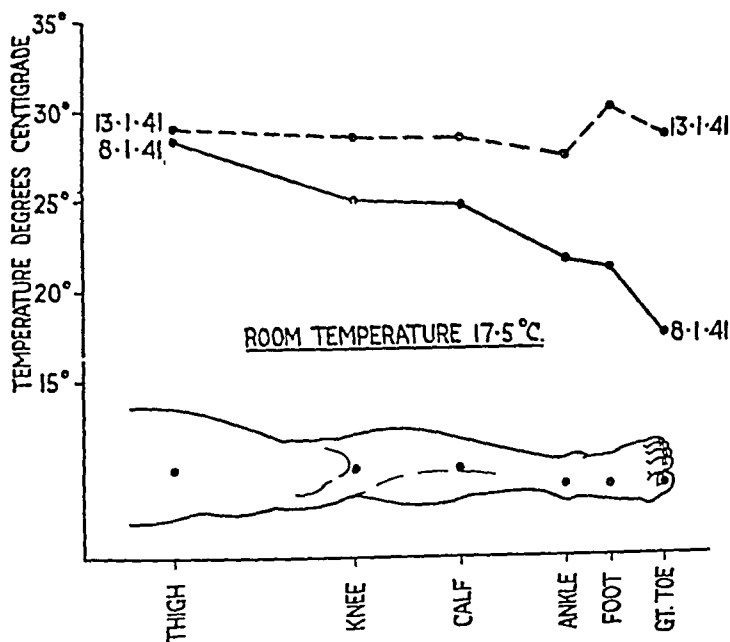


FIG. 17.—Diagram to show improvement in cutaneous temperature of left leg following conservative therapy in case of pseudo-embolism.

blocked the left popliteal artery, and the foot became cold, powerless and pulseless. On account of her general condition conservative measures were employed—anticoagulants were not available—and three days later there was adequate circulation in the foot; although the pulses had not returned, the skin temperatures on the affected side were slightly higher than on the other, indicating the patency and dilatation of the subcutaneous collaterals. Eight days after the onset, the whole leg was warmer, and the pulses in the foot were palpable (Fig. 17). Eleven days after the original episode she suddenly became unconscious, with Jacksonian twichings on the left side: a diagnosis of cerebral embolism was made, and shortly afterwards she died. At autopsy the pathologist could not find emboli either in the cerebral or in the peripheral arteries.

A man aged 55 was admitted to Dr W. D. D. Small's wards, after an attack of coronary thrombosis. After 18 days he had what was clinically an infarct

of the spleen. On the following day the left leg became pale, powerless and pulseless below the knee. Three hours after onset the femoral pulse was not palpable beyond a point 2.5 cm. distal to the inguinal ligament. He was given heparin and reflex vasodilatation was established. After two hours the popliteal pulse was palpable and the foot was warm. Mr A. J. Slessor, who was looking after him, wisely decided to continue with conservative measures. The next day the pulses in the foot were still absent, but there was no evidence of impending nutritional disturbance, either cutaneous or muscular. During the next 15 days the peripheral pulses came and went in *both* feet; and on the 7th and 8th days there were two curious episodes, during which the right thumb became painful, cold and weak. During these episodes, the radial pulse was absent, but it could be made to reappear by rolling the distal segment of the brachial artery or the proximal segment of the radial artery under the fingers. The radial artery was obviously in temporary spasm. This method of relaxing such a spastic artery had been suggested by Mayo in 1837, and was confirmed by MacWilliam in 1901. It is to be compared with the fall in blood pressure readings in hypertensives which may follow repeated inflation and deflation of the cuff of the sphygmomanometer.

My present attitude towards the treatment of peripheral emboli is that, if the patient is seen within say ten hours, one should await the result of treatment with heparin. If this is to be of value, unmistakable improvement will appear within about two hours. I do not think this time is lost; if after an unprofitable interval embolectomy is performed, there may be a somewhat better chance of preserving local function, but the ultimate result will depend more upon the exact site of arterial obstruction and upon the architecture of the arterial tree in each particular patient. Details of technique are out of place in a lecture such as this; but the analysis of my case-histories leads me to emphasise one point in the management of arterial embolism. It is not by any means an original observation: indeed it was enunciated more than a century ago by Dupuytren:—

“We should never lose sight of the importance of preserving whilst we are curing.”

I thank those of my colleagues who have asked me to see or deal with these cases. I am greatly indebted to a series of junior colleagues who have made observations and documented the cases: Dr R. L. Richards, Dr C. C. Burt and Mr A. J. Slessor. Success in operations has been vastly helped by Sister Gordon in the operating theatre and Sisters Sutton and McWhir in the wards.

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## PRESIDENTIAL ADDRESS

### A COMPARISON OF MATERNITY HOSPITAL RECORDS DURING THE LAST TWENTY YEARS AS A BASIS FOR THOUGHTS FOR THE FUTURE IMPROVEMENT OF MIDWIFERY

By Dr W. F. T. HAULTAIN,  
O.B.E., M.C., F.R.C.P.E., F.R.C.S.E., F.R.C.O.G.

I HAVE to thank you for the honour you did me a year ago in electing me President of this old and venerable Society and in re-electing me to-night. It is an honour which I value very highly, not only personally, but also familiarly as my father was similarly honoured in 1910-11, this being the first occasion in the annals of the Society when both a father and a son have been so honoured.

It behoves a man at intervals in his lifetime to ponder and take stock of himself in order to ascertain how he is progressing; what he might have done in the past to have fared better; and what improvements he should try to effect for his future. If this is necessary for each of us personally how much more essential is it for any great hospital to do the same, for its work is of so much more importance and so much greater is its influence. I propose therefore to-night to look at the records of a hospital, which is dear to all of us here, namely "the Simpson," in order to try and estimate the work that has been carried out at both the old and the new hospitals in the last twenty years, during which time it has been my good fortune to be in intimate association with it. I hope, in the first place, to show that great improvements have taken place during this period, and in so doing would desire to compare its work with other great maternity hospitals in this country and abroad; in the second place I will try to determine how these results have been achieved; and finally I would like to look to the future and give my views as to how further improvement in midwifery might be achieved in this country; this would seem to be of especial importance at the present time when the country is embarking on a new National Health Service Scheme, in which midwifery plays an important part.

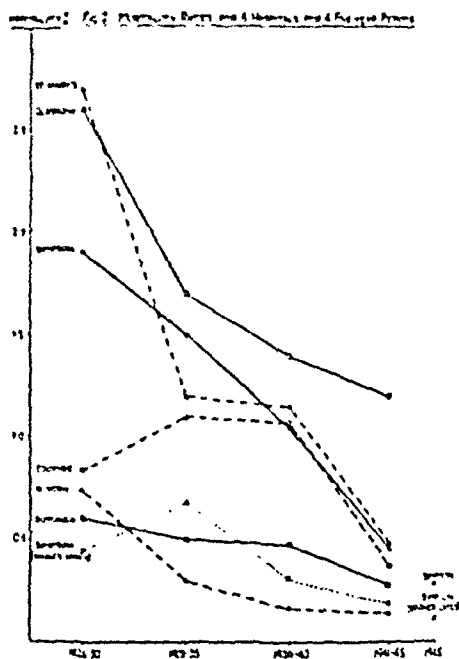
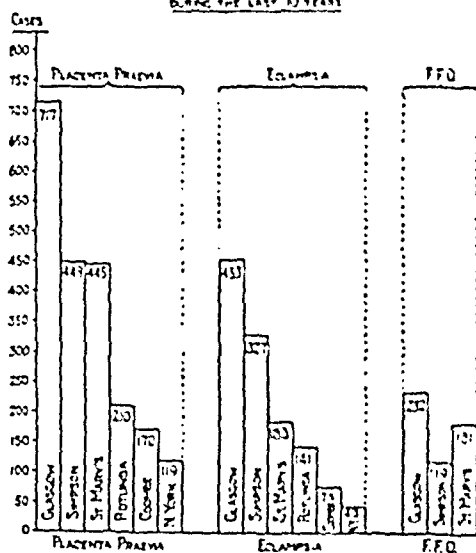
The hospitals which I have selected for comparison with our own are the Royal Maternity Hospital, Glasgow; St Mary's Hospital, Manchester; the Rotunda and Coombe Hospitals in Dublin, and the New York Lying-in Hospital. These hospitals all serve large areas but their emergency admissions vary in numbers and in severity: for instance, in the Glasgow Hospital 55-60 per cent. are emergency cases, at St Mary's 55 per cent., at the Simpson 25 per cent., at the Rotunda and Coombe about 20 per cent., and at the New York Lying-in Hospital much fewer, as they appear to admit only booked cases or emergency cases from their own district. The number of

emergency cases is of great significance and importance and will be referred to later in connection with the statistics. An indication of the numbers and types of abnormal conditions dealt with in the various hospitals during the past ten years is shown in Fig. 1.

The figures for failed forceps are not given in the case of the Rotunda, Coombe and New York hospitals.

It is well recognised that the admission of non-booked cases to a hospital raises the maternal mortality and morbidity rates in comparison with hospitals which admit only from their own ante-natal cases, a fact which can also be seen by comparing the greatly decreased mortality and morbidity in the booked cases (*i.e.* those who have attended the hospital ante-natal clinics before admission) with the total mortality and morbidity of the hospital, or even more so with

FIG. 1. COMPARISON OF HOSPITALS WITH REGARDS TO SOME ABNORMALITIES DURING THE LAST 10 YEARS



that of the "non-booked" cases. This is very clearly seen in the maternal mortality graphs of the Simpson (Fig. 2). You will note that for 1945 the mortality rate is 0.28 per cent. for all cases, but is only 0.12 per cent. for booked cases, the lowest rate the Simpson had ever achieved.

The efficiency and obstetric reputation of a maternity hospital are primarily judged by its maternal mortality and morbidity and by its still-birth and neo-natal death rates. If therefore these rates show a marked decrease in the past twenty years then one can justifiably assume that the hospital's work has progressed. The graphs of these rates for the various hospitals for five-yearly periods, beginning in 1926 and ending in 1945, to which I would now draw your attention, would appear to give striking evidence as to the progress midwifery has made during these years, for in every case these rates are definitely lowered. Though the mortality statistics of the New York Lying-in

Hospital seem to put the British hospitals to shame, it must be pointed out that most of the New York cases come under the "booked" category, and the figures for the Simpson "booked" cases for 1945 approach those of New York quite closely.

Morbidity for the British and Irish hospitals (Fig. 3) has been gauged by the B.M.A. standard, but the standard for the Lying-in Hospital, New York, is more strict as the temperature is taken four-hourly and this probably accounts for the higher rate. These graphs show how morbidity has decreased in all the hospitals.

The neo-natal and still-birth rate (Fig. 4) has also decreased though not so noticeably, and there is reason to suppose, as far as the Simpson is concerned, that the figure for 1926-30 is not exactly comparable with those of the other periods, as the statistics were more exactly

FIG. 3. Morbidity Rates in Six Hospitals

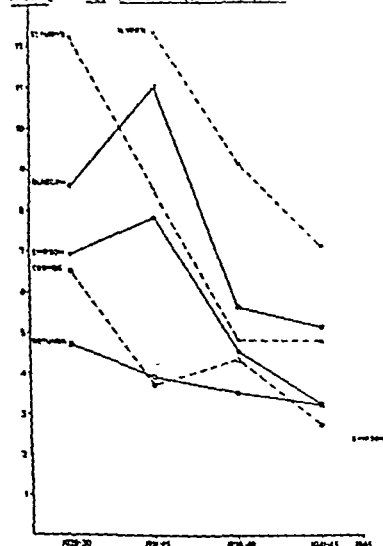
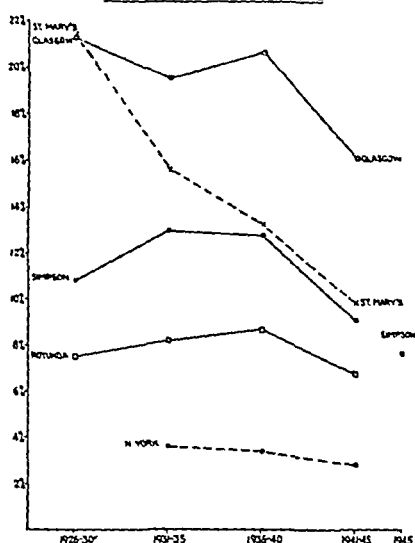


FIG. 4

STILLBIRTHS AND NEONATAL DEATHS  
PERCENTAGE OF ALL CASES AT FIVE HOSPITALS



prepared after that date, when the pædiatrician took charge of these records. I do not propose to touch on these last figures to-night as such a discussion would take up too much time and could easily be the subject for a separate paper. However, I would like to record that in my opinion the improvement at the Simpson has been achieved principally by the advent of a pædiatrician, to his gentle methods of insinuation, permeation and infiltration, which with some difficulty overcame all the obstetricians' scruples and forebodings, and which in 1939 gave him and his associates full control of the babies both healthy and unhealthy. We as a staff, and Edinburgh and the South-east of Scotland as an area, are greatly beholden to Professor Charles McNeil, the first occupant of the chair of Child Life and Health in the University, for his pioneer work in our midst, a result he could not have achieved without having spent a considerable part of his valuable time in attending daily the nurseries of the



hospital. This pioneer work has been duly acclaimed by the whole country.

Accepting that midwifery in these hospitals has improved generally, I now propose to determine how such improvement has been achieved. In order to do this I have put in your hands tables of the main causes of death in these hospitals for five-yearly periods 1926-30, 1931-35, 1936-40 and 1941-45 (Tables I-VI). These show in the first place how the hospitals compare with one another in regard to the numbers of deaths, arranged according to main causes; secondly, how the totals of deaths from the various causes have decreased in the successive quinquennial periods; and thirdly, how the totals of each cause of death related in percentage to the total admissions have fallen.

The majority of maternal deaths come under three main headings; (1) Sepsis, (2) Toxæmia and (3) Hæmorrhage, and Table VII shows a comparison of the percentage in the hospitals studied of deaths under these three headings occurring during the last ten years; and also figures for some American hospitals, as well as the total percentage for U.S.A. for 1941. To these three main causes of death must be added cardiac lesions, which also cause many maternal deaths in all the hospitals, and uterine rupture, deaths from which are not without significance. It is impossible to-night to go into all these tables in detail, but perhaps they may give you food for attention and thought at your leisure.

Let us now examine the main causes of maternal mortality individually and in more detail to try and advance reasons for any improvement, which has been achieved. I would propose in the first place to discuss sepsis.

### SEPSIS

By reference to Table VIII and Graphs 5 and 5a, it will be seen that the incidence of puerperal sepsis has decreased in all the hospitals with the exception of the Rotunda and that the deaths from sepsis have also decreased with the exception of Glasgow where they have remained stationary for the past fifteen years. It is interesting to note that though the morbidity rate in the New York Lying-in Hospital is higher than that of our hospitals, there has been no death from sepsis in that hospital during the last five years, an achievement which deserves the highest praise. It might be of passing interest to record that at the Simpson during the year 1936 every patient after delivery received a dose of calcium sulphide gr. ij t.i.d. for four days, and during that year the morbidity, which had previously never been lower than 6 per cent. (usually between 7-8 per cent.) dropped to 4.3 per cent. During the following year every patient had prophylactic sulphonamide for three days after delivery and the morbidity dropped further to 3.4 per cent., which was the lowest figure recorded, even though we moved into the new hospital in 1939, until the years 1944 and 1945, when the morbidity was reduced to 2.9 per cent. and 2.2 per cent. respectively.

What are the causes of this general improvement in morbidity and deaths from sepsis? It has come when our country was in the throes of war, when food was scarce and many of the cities had suffered greatly from bombing. The people would therefore be expected to be undernourished, over-anxious, and an easy prey to infection; during the whole period the hospital staffs were severely depleted and overworked and the hospitals grossly overcrowded; a completely aseptic technique was impossible to achieve owing to the shortage of materials and at the Simpson gloves had not been worn, except for caesarean sections, since 1942, as they were unobtainable in sufficient quantity. It is remarkable therefore that for the years 1944-45 when circumstances were absolutely at their worst there

FIG. 5. SEPSIS—MORTALITY % OF TOTAL ADMISSIONS FOR 6 HOSPITALS

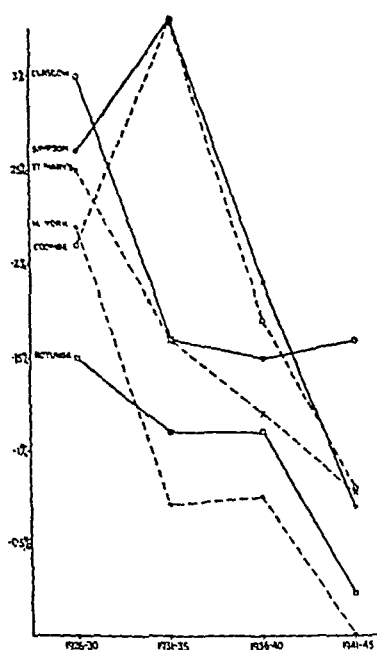
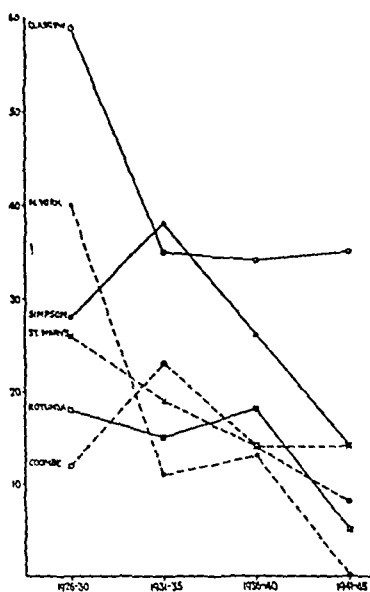


FIG. 5A. SEPSIS—NUMBER OF DEATHS IN 6 HOSPITALS



were only two deaths from sepsis at the Simpson. It is indeed difficult to reconcile these facts, but I think improvement may have been due to several causes:—(1) The use of *sulphonamides* prophylactically in cases liable to infection and curatively in cases of infection. It will be seen, however, from Table VIII that, with the exception of the Rotunda and to a lesser extent of the Simpson, though the number of cases of sepsis is markedly diminished, if the patient does develop sepsis, the mortality percentage is not reduced. It is to be hoped that the administration of penicillin may have a beneficial effect on many of the cases which resist sulphonamide treatment, and that in the next five years the mortality rate will be greatly reduced. (2) *Dietetic*. The privilege of the pregnant woman to obtain one extra pint of milk a day as well as Vitamins A, D and C, all of which could

TABLE I—PRINCIPAL CAUSES OF DEATH (IN ORDER OF FREQUENCY)  
*The Simpson, Edinburgh*

1926-30.				1931-35.				1936-40.				1941-45.			
TOTAL ADMISSIONS—10,749				11,652				13,372				18,640			
Cause.	Number.	Percentage of Admissions.		Cause.	Number.	Percentage of Admissions.		Cause.	Number.	Percentage of Admissions.		Cause.	Number.	Percentage of Admissions.	
Eclampsia	50	0·46		Sepsis	38	0·33		Sepsis	26	0·19		Eclampsia	15	0·08	
Sepsis	28	0·26		Cardiac	19	0·16		Eclampsia	15	0·11		Sepsis	14	0·07	
Pre-eclampsia	14	0·13		Eclampsia	15	0·13		Pre-eclampsia	13	0·09		Cardiac	9	0·05	
Rupture	14	0·13		Pre-eclampsia	15	0·13		P.P.H. and Shock	13	0·09		P.P.H. and Shock	8	0·05	
Pl. Prævia	12	0·11		P.P.H. and Shock	11	0·09		Cardiac	11	0·08		Rupture	4	0·02	
Hyperremesis	12	0·11		Pl. Prævia	11	0·09		Hyperremesis	9	0·07		Pl. Prævia	2	0·01	
Cardiac	11	0·10		Hyperremesis	8	0·07		Pl. Prævia	8	0·06		Pre-eclampsia	2	0·01	
P.P.H. and Shock	8	0·07		Rupture	8	0·07		Rupture	6	0·04		Acc. Hæm.	1	0·005	
Acc. Hæm.	7	0·06		Acc. Hæm.	3	0·03		Ret. Placenta B.B.O.	6	0·04		Hyperremesis	0	...	
Ret. Placenta B.B.O.	2	0·02		Ret. Placenta B.B.O.	1	0·009		Acc. Hæm.	4	0·04		Ret. Placenta B.B.O.	0	...	

TABLE II—PRINCIPAL CAUSES OF DEATH (IN ORDER OF FREQUENCY)  
*Glasgow R.M.II.*

1926-30.				1931-35.				1936-40.				1941-45.			
TOTAL ADMISSIONS—19,806				22,433				23,113				21,944			
Cause.	Number.	Percentage of Admissions.		Cause.	Number.	Percentage of Admissions.		Cause.	Number.	Percentage of Admissions.		Cause.	Number.	Percentage of Admissions.	
Eclampsia	64	0·32		Eclampsia	51	0·23		P.P.H. and Shock	44	0·19		P.P.H. and Shock	37	0·17	
Sepsis	59	0·30		Sepsis	35	0·10		Eclampsia	35	0·15		Sepsis	35	0·16	
Pl. Prævia	52	0·26		Pl. Prævia	31	0·14		Sepsis	34	0·15		Eclampsia	34	0·15	
Pre-eclampsia	43	0·20		Cardiac	31	0·14		Cardiac	29	0·13		Cardiac	24	0·11	
Hyperremesis	38	0·15		Acc. Hæm.	31	0·14		Acc. Hæm.	20	0·09		Ret. Placenta B.B.O.	24	0·11	
Cardiac	34	0·17		P.P.H. and Shock	18	0·08		Hyperremesis	19	0·08		Rupture	17	0·075	
Acc. Hæm.	26	0·13		Hyperremesis	18	0·08		Rupture	18	0·08		Acc. Hæm.	14	0·06	
P.P.H. and Shock	20	0·1		Pre-eclampsia	16	0·07		Ret. Placenta B.B.O.	17	0·07		Pl. Prævia	12	0·05	
Rupture	17	0·09		Ret. Placenta B.B.O.	15	0·06		Pre-eclampsia	14	0·06		Pre-eclampsia	7	0·03	
Ret. Placenta B.B.O.	16	0·08		Rupture	14	0·05		Pl. Prævia	12	0·05		Hyperremesis	7	0·03	

TABLE III—PRINCIPAL CAUSES OF DEATHS (IN ORDER OF FREQUENCY)  
*St Mary's Hospital, Manchester*

	1936-30.			1931-35.			1936-40.			1941-45.		
	Cause.	Number.	Percentage of Admissions.	Cause.	Number.	Percentage of Admissions.	Cause.	Number.	Percentage of Admissions.	Cause.	Number.	Percentage of Admissions.
TOTAL ADMISSIONS—10,178		26	0.25		25	0.21		24	0.20		14	0.077
Sepsis . . .	P.P.H. and Shock	26	0.25	Sepsis . . .	19	0.16	Eclampsia . . .	18	0.15	Sepsis . . .	12	0.066
P.P.H. and Shock				Eclampsia . . .	18	0.15	Pre-eclampsia . . .	17	0.14	Eclampsia . . .	10	0.055
Cardiac . . .				Cardiac . . .	13	0.11	Cardiac . . .	16	0.13	P.P.H. and Shock	10	0.055
Eclampsia . . .				Acc. Hæm. . .	13	0.11	Sepsis . . .	14	0.12	Pl. Prævia . . .	7	0.038
Pl. Prævia . . .				Pre-eclampsia . . .	12	0.10	Hyperemesis . . .	12	0.10	Pre-eclampsia . . .	2	0.011
Acc. Hæm. . .				Pl. Prævia . . .	9	0.08	Acc. Hæm. . .	11	0.09	Ret. Placenta . . .	2	0.011
Hyperemesis . . .				Hyperemesis . . .	7	0.06	Pl. Prævia . . .	6	0.05	B.O. . . . .	1	0.006
Ret. Placenta . . .				Ret. Placenta . . .	6	0.05	Ret. Placenta . . .	6	0.05	Acc. Hæm. . .	1	0.006
B.O. . . . .				B.O. . . . .			Rupture . . .	3	0.025			
Pre-eclampsia . . .				Rupture . . .	2	0.02						
Rupture . . .												

TABLE IV—PRINCIPAL CAUSES OF DEATHS (IN ORDER OF FREQUENCY)  
*Rotunda*

	1936-30.			1931-35.			1936-40.			1941-45.		
	Cause.	Number.	Percentage of Admissions.	Cause.	Number.	Percentage of Admissions.	Cause.	Number.	Percentage of Admissions.	Cause.	Number.	Percentage of Admissions.
TOTAL ADMISSIONS—11,914		18	0.15		15	0.11		18	0.11		10	0.047
Sepsis . . .				Sepsis . . .	8	0.056	Sepsis . . .	11	0.065	Eclampsia . . .	6	0.028
Eclampsia . . .				Eclampsia . . .	8	0.056	Acc. Hæm. . .	9	0.053	Rupture . . .	5	0.023
P.P.H. and Shock				P.P.H. and Shock	6	0.04	Eclampsia . . .	8	0.046	Sepsis . . .	5	0.023
Cardiac . . .				Cardiac . . .	6	0.04	P.P.H. and Shock	5	0.03	Pre-eclampsia . . .	4	0.019
Pre-eclampsia . . .				Pre-eclampsia . . .	4	0.028	Pl. Prævia . . .	3	0.018	Cardiac . . .	4	0.019
Acc. Hæm. . .				Acc. Hæm. . .	4	0.028	Pre-eclampsia . . .	3	0.018	P.P.H. and Shock	3	0.014
Pl. Prævia . . .				Pl. Prævia . . .	4	0.028	Rupture . . .	2	0.012	Acc. Hæm. . .	3	0.014
Rupture . . .				Rupture . . .	2	0.01	Hyperemesis . . .	1	0.006	Pl. Prævia . . .	3	0.014
Hyperemesis . . .				Hyperemesis . . .	2	0.01	Ret. Placenta . . .	1	0.006	Hyperemesis . . .	1	0.003
Pl. Prævia . . .				Hyperemesis . . .	2	0.01	B.O. . . . .					

TABLE V—PRINCIPAL CAUSES OF DEATHS (IN ORDER OF FREQUENCY)  
*Coombe Hospital, Dublin*

1926-30. TOTAL ADMISSIONS—5619			1931-35. 7010			1936-40. 8189			1941-45 9965		
Cause.	Number.	Percentage of Admissions.	Cause.	Number.	Percentage of Admissions.	Cause.	Number.	Percentage of Admissions.	Cause.	Number.	Percentage of Admissions.
Sepsis	12	0·21	Sepsis	23	0·33	Sepsis	14	0·17	Sepsis	8	0·08
Pl. Prævia	8	0·14	Pl. Prævia	5	0·07	Cardiac	9	0·11	P.P.H. and Shock	5	0·05
Cardiac	4	0·07	Acc. Hem.	5	0·07	Acc. Hem.	7	0·09	Acc. Hem.	3	0·03
Acc. Hem.	4	0·07	Cardiac	4	0·06	P.P.H. and Shock	7	0·09	Pl. Prævia	2	0·02
P.P.H. and Shock	4	0·07	Eclampsia	4	0·06	Pl. Prævia	6	0·07	Eclampsia	2	0·02
Hyperemesis	4	0·07	P.P.H. and Shock	4	0·06	Eclampsia	5	0·06	Rupture	1	0·01
Eclampsia	3	0·05	Hyperemesis	3	0·04	Hyperemesis	4	0·05			
Rupture	2	0·04	Rupture	2	0·03	Pre-eclampsia	4	0·05			
						Rupture	1	0·01			

TABLE VI—PRINCIPAL CAUSES OF DEATHS (IN ORDER OF FREQUENCY)  
*New York Lying-in Hospital*

1926-30. TOTAL ADMISSIONS—17,790			1931-35. 14,166			1936-40. 17,501			1941-45. 19,763		
Cause.	Number.	Percentage of Admissions.	Cause.	Number.	Percentage of Admissions.	Cause.	Number.	Percentage of Admissions.	Cause.	Number.	Percentage of Admissions.
Sepsis	40	0·22	Sepsis	11	0·07	Sepsis	13	0·07	Embolus	6	0·03
P.P.H. and Shock	18	0·10	P.P.H. and Shock	5	0·04	Cardiac	6	0·03	Cardiac	4	0·02
Cardiac	13	0·07	Embolus	4	0·03	P.P.H. and Shock	4	0·024	P.P.H. and Shock	2	0·01
Pre-eclampsia	12	0·07	Acc. Hem.	3	0·02	Cerebro-vasc.	3	0·017	Cerebro-vasc.	2	0·01
Rupture	10	0·06	Cardiac	2	0·01	Embolus	3	0·017			
Eclampsia	7	0·04	Rupture	2	0·01	Acc. Hem.	2	0·012			
Embolus	4	0·02	Pre-eclampsia	2	0·01	Hyperemesis	2	0·012			
Acc. Hem.	2	0·01	Eclampsia	1	0·007	Pl. Prævia	1	0·006			
						Rupture	1	0·006			
						Eclampsia	1	0·006			

TABLE VII  
Percentage of the Total Deaths, 1936-45

	Sepsis.	Toxæmia.	Hamorrhage.
Simpson	18.2 (25.2)	24.5 (30.7)	19.9 (14.8)
Glasgow R.M.H.	11.7 (10.3)	19.7 (25.2)	30.6 (21.8)
St Mary's	13.3 (12.2)	22.1 (20.1)	29.2 (27.9)
Rotunda	18.0 (23.2)	23.4 (25.8)	27.3 (19.6)
Chicago Lying-in	39.5	7.4	16.0
Cook County Hospital	23.5	17.6	12.6
N.Y. Lying-in	19.4 (30.9)	4.5	13.4 (16.9)
U.S.A. (1941)	38	25	25
Brooklyn (8 years)	150 cases	110 cases	208 cases

Figures in brackets indicate previous 10-year (1926-35) percentage.

TABLE VIII—MORTALITY STATISTICS FOR SEPSIS

	1926-30.	1931-35.	1936-40.	1941-45.
Total Cases.	372	Total Cases.	Total Cases.	Total Cases.
Simpson	28	486	333	265
Glasgow R.M.H.	59	2533	1120	901
St Mary's	26	989	571	582
Rotunda	18	465	498	617
Deaths.		Deaths.	Deaths.	Deaths.
		38	26	14
		35	34	35
		19	14	14
		15	18	5
Percentage.		Percentage.	Percentage.	Percentage.
	7.5	7.8	7.8	5.3
	3.9	1.4	3.0	3.9
	2.4	1.9	2.4	3.4
	4.1	3.2	3.6	0.8

TABLE IX—MORTALITY STATISTICS FOR ECLAMPSIA

	1926-30.	1931-35.	1936-40.	1941-45.
Total Cases.	177	Total Cases.	Total Cases.	Total Cases.
Simpson	50	135	150	177
Glasgow R.M.H.	64	388	230	223
St Mary's	17	129	89	94
Rotunda	13	55	55	86
Coombe	3	34	46	30
Deaths.		Deaths.	Deaths.	Deaths.
		15	15	15
		51	35	34
		18	18	10
		8	9	10
		4	5	2
Percentage.		Percentage.	Percentage.	Percentage.
	28.2	11.1	10	8.5
	16.2	15	(B 5.4)	(B 3.4)
	9.8	13.9	15.2	15.2
	21.7	14.8	20.2	10.6
	15.4	11.8	16.4	11.6
			10.9	6.7

be obtained free of charge has helped considerably; as other food was scarce and the pregnant woman realised she was obtaining something which no one else could get, she took full advantage of these supplements, which, though available, she had never accepted previously. (3) *Early visits* by all pregnant women to their doctors or ante-natal clinics were necessary to get the certificate for their extra milk and vitamins besides extra coupons for clothing, and the milk certificates had to be renewed at frequent intervals; so that every pregnant woman received early and efficient ante-natal care, which many would not have troubled to obtain if there had been no certificates to be signed. Thus during the war there has been achieved generally and without any difficulty, a virtual notification of pregnancy, the mere suggestion of which previously had led to much bitter and acrimonious controversy. (4) As the general practitioners were so overworked, few had the time or the inclination to undertake midwifery, so that in the main ante-natal care was carried out at clinics or by practitioners keen on midwifery; thus the patients came under skilled observation throughout pregnancy. (5) As nurses were scarce and home helps impossible to obtain, nearly every primipara was *delivered in hospital* or in a nursing-home, and thus the number of infected non-booked cases admitted were greatly reduced. (6) In this connection also the effect of the *intensive midwifery instruction of the students*, which had been carried out for about fifteen years previously was beginning to bear fruit and the practitioner, realising his limitations, sent the difficult case immediately into hospital, thus avoiding dangerous interference in the patient's own home. (7) An important part has been played by *improvement in technique* such as the more frequent use of the lower uterine segment caesarean section, and of blood transfusion, the introduction of dettol as an antiseptic, the wearing of masks, and, at the Simpson, the better administration of anæsthetics by well-qualified resident anæsthetists, who were always available for difficult cases. The complete segregation of clean and possibly infected cases, which became feasible in 1939 when the new Simpson Pavilion was opened does not seem to have had such a beneficial effect as was anticipated for it was not until after two to three years' occupation that the morbidity rate decreased appreciably, the figures for the seven years after its occupation being 4.95, 5.86, 2.8, 4.1, 4.0, 2.9 and 2.2 per cent.

#### TOXÆMIA

De Lee once stated that ante-natal care had diminished the incidence of eclampsia, but as far as the British hospitals are concerned this reduction has occurred only in Glasgow and St Mary's, and even they treated 223 and 94 cases respectively during the last five-year period. In fact toxæmia still accounts for a large proportion of maternal deaths both in Britain and U.S.A. as is shown in the Tables I-VII. Though the general incidence of eclampsia has disappointingly not altered very much, there has been a decrease in the mortality rate

in most hospitals, this being especially noteworthy in the Simpson and the Rotunda, whilst the number of deaths has been substantially decreased in Glasgow; it will be noted that for the last five-year

FIG. 6. ECLAMPSIA - NUMBER OF CASES IN FIVE HOSPITALS

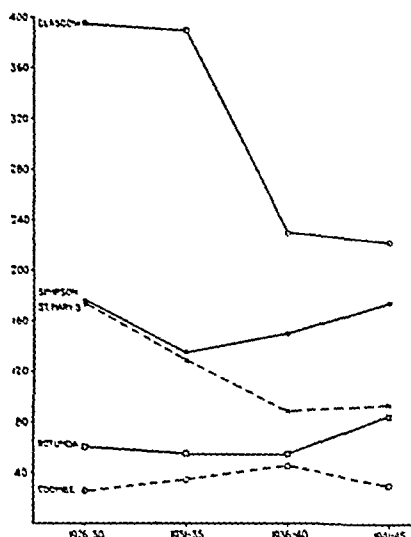


FIG. 6A. ECLAMPSIA - NUMBER OF DEATHS IN SIX HOSPITALS

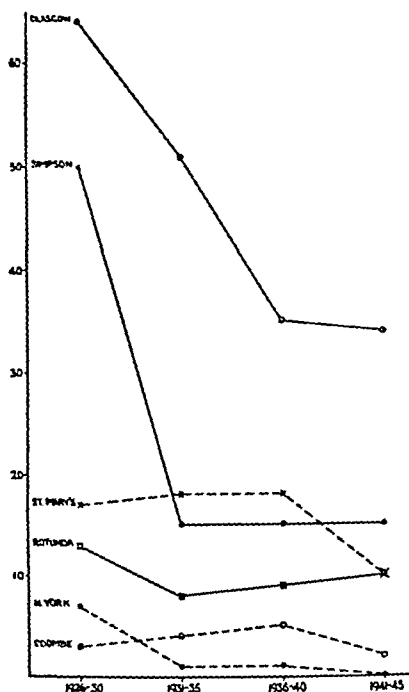
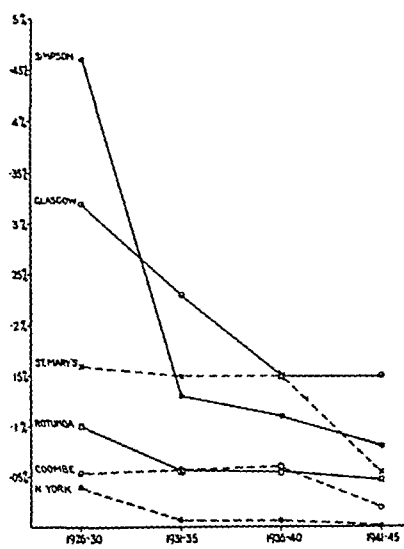


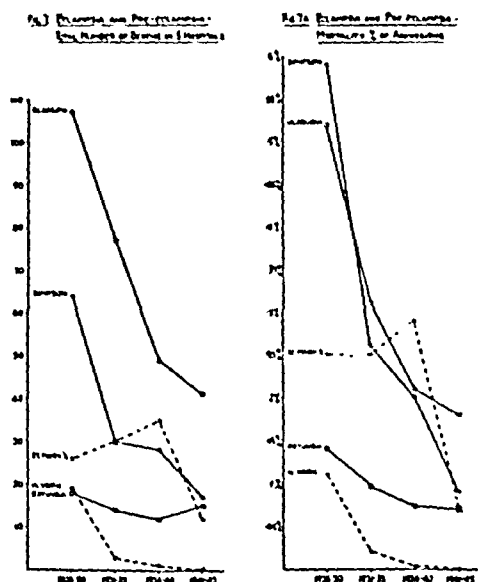
FIG. 6B. ECLAMPSIA - MORTALITY % OF ALL ADMISSIONS AT 6 HOSPITALS



period the mortality rate for the Simpson is the lowest yet recorded namely 8.5 per cent. At all the hospitals (Figs. 6, 6a and 6b; Table IX) the percentage mortality from eclampsia related to the total



number of admissions has diminished for each quinquennial period, but this has little significance in Scotland as the total number of cases of eclampsia admitted yearly has not decreased since 1930. It is of interest to compare these figures with those of the Boston Lying-in Hospital, where the mortality rate from 1940 to 1944 was 13·5 per cent., which is definitely higher than the Simpson and slightly lower than Glasgow. It was once surmised that the reason there was practically no eclampsia in Germany during the final years of the 1914-18 war, though it had been prevalent previously, was because the population was on a starvation diet and there was very little consumption of protein. It would seem that this conjecture is fallacious as the protein available in Britain since 1942 has been very small and yet the incidence of eclampsia has not varied.



One cannot consider eclampsia, however, without also considering pre-eclampsia, eclampsism or profound toxæmia without convulsions, call it what you will ; if the mortality from eclampsia and profound toxæmia are considered together it will be seen (Figs. 7 and 7a ; Table X) that the mortality has decreased very considerably in all the hospitals with the exception of the Rotunda, where the mortality has remained pretty stationary at about three deaths a year, which number is rather less than in the British hospitals quoted. In order to try and find a cause for this marked decrease in mortality I have made a detailed study (Table XI) of the Simpson statistics of pre-eclampsia during the twenty years and it would appear therefrom that the principal reasons are (1) the increased admission of pre-eclamptic cases, 1592 cases being admitted from 1941-45 as against 627 from 1926-31, due firstly to practitioners appreciating the treacherous nature of pre-eclampsia and the value of hospitalisation to permit of constant supervision, and secondly to the increased ante-natal bed accommodation in the new pavilion, which made this possible, and (2) the increasing

TABLE X—MORTALITY IN ECLAMPSIA AND PRE-ECLAMPSIA

	1936-39.			1931-35.			1926-30.			1916-20.			1911-15.		
	Total	Percentage of		Total -	Percentage of		Total	Percentage of		Total	Percentage of		Total	Percentage of	
	Deaths.	all Deaths.	Admissions.	Deaths.	all Deaths.	Admissions.	Deaths	all Deaths.	Admissions.	Deaths	all Deaths.	Admissions.	Deaths	all Deaths.	Admissions.
Simpson	64	33	0.59	30	17	0.26	28	20.2	0.2	17	20.5	0.09			
Glasgow R.M.H.	107	20.4	0.52	77	17.3	0.31	49	15.3	0.2	41	15.2	0.18			
St Mary's	26	12.7	0.25	30	18.3	0.25	35	23.9	0.3	15	15	0.07			
Rotunda	18	24.6	0.14	14	20.2	0.1	12	16.7	0.07	15	26.7	0.07			
N.Y. Lying-in	19	14.1	0.11	3	10	0.02	1	2.2	0.002		Nil				

TABLE XI—PRE-ECLAMPSIA

*Mortality Rates and Treatments, The Simpson, 1926-45*

	1926-30.	1931-35.	1936-40.	1941-45.
Cases admitted . . . . .	627	712	1107	1592
Deaths . . . . .	14	15	13	2
Percentage Mortality . . . . .	2·2	2·1	1·2	0·13
Percentage Deaths for all admissions . . . . .	0·13	0·13	0·08	0·01
<i>Treatments adopted—</i>				
Induction Labour . . . . .	125	317	514	672
Cæsarean Section . . . . .	10	23	56	88
Abdominal Hysterotomy . . . . .	4	5	15	13
Induction Abortion . . . . .	4	7	7	2

*Treatments adopted—*

Induction Labour . . . . .	125	317	514	672
Cesarean Section . . . . .	10	23	56	88
Abdominal Hysterotomy . . . . .	4	5	15	13
Induction Abortion . . . . .	4	7	7	2

TABLE XII--MORTALITY STATISTICS FOR PLACENTA PRÆVIA

	1936-30.			1931-35.			1936-40.			1941-45.		
	Total Cases.	Deaths.	Percentage.	Total Cases.	Deaths.	Percentage.	Total Cases.	Deaths.	Percentage.	Total Cases.	Deaths.	Percentage.
Simpson	189	12	6·3	208	11	5·3	214	8	3·9	235	2	0·9
Glasgow R.M.H.	419	52	12·4	490	31	6·3	504	12	2·4	413	12	2·9
St Mary's	267	13	4·9	233	9	3·9	175	6	3·4	270	7	2·6
Rotunda	103	1	0·9	66	4	6·1	57	5	8·5	153	3	2·0
Coombe	47	8	17	65	5	7·7	81	6	7·4	89	2	2·3

number of pregnancies terminated by the induction of premature labour, caesarean section or even abdominal hysterotomy during each successive five-year period. Everlasting vigilance and wary alacrity are necessary if pre-eclampsia is to be managed successfully and earlier termination of pregnancy has been extensively recommended to improve the results. These opinions are well corroborated by the Simpson figures, for in the first five years for 627 cases of pre-eclampsia 125 labours and 4 abortions were induced and 14 abdominal sections were performed, whereas in the last five years for 1592 cases of pre-eclampsia 672 labours and 2 abortions were induced and 101 abdominal sections were done. By such treatments the mortality from pre-eclampsia has decreased from 14 deaths (2.2 per cent. mortality) between the years 1926-30, to 2 deaths (0.13 per cent. mortality) in the 1941-45 period, and it is impossible to surmise how many cases of eclampsia were prevented.

The mortality tables show very definitely that one toxæmia which gave great cause for anxiety in the past, namely hyperemesis gravidarum, does not cause the same concern now, Glasgow being the only hospital to show even an appreciable number of deaths during 1941-45, namely 7. In the Simpson there has been no death from this cause during the last period and at St Mary's there was only one death recorded; even in Glasgow the total deaths from this cause have dropped from 38 in 1926-30 to 7 in 1941-45. Why has this occurred? From my experience here I consider that it is due (1) to the early visit to a doctor or clinic, so as to get the extra ration book and clothing coupons thus bringing the patients under observation much earlier than previously, and (2) to the better instruction of medical students as to the significance of vomiting in early pregnancy; the Simpson statistics show clearly the value that has been derived from such instruction, as there were 29 toxic cases of hyperemesis treated in 1926-30 with 12 deaths, 43 in the next five years with 8 deaths, 62 for the next five years with 9 deaths but only one toxic case was treated and that successfully, during the war years. During this last period 130 cases of hyperemesis of moderate severity were admitted as compared with an average of 290 for the other quinquennial periods. This diminution may also partly be due to the pregnant woman having had plenty to occupy her time and thoughts during the war years and thus the neurotic factor was to some extent eliminated.

### HÆMORRHAGE

Under this heading I have included post-partum hæmorrhage and obstetric shock, cases admitted after delivery outside with the placenta still *in situ*, which I have called in the tables retained placenta B.B.O. (baby born outside), placenta prævia, and, rightly or wrongly, accidental hæmorrhage, some of which cases should better have been classified under toxæmia. By referring again to Table VII, it will be seen that for the British and Irish hospitals, with the exception of the Simpson,

hæmorrhage has caused the highest proportion of maternal deaths during the last ten years. In Glasgow this is partly due to the number of cases sent in after delivery outside with the placenta still *in situ*, no fewer than 41 deaths being from this cause. Post-partum hæmorrhage and shock account for 81 deaths in the Glasgow Maternity Hospital during the past ten years, being the principal cause of maternal mortality. (Figs. 8 and 8a). In the Simpson for the same period the number of deaths from these two causes is 21 and is only the fourth highest cause of death. It is difficult to account for this high mortality, but it is probably due to (1) the admission of almost moribund cases; (2) the necessity for prolonged anæsthesia for difficult deliveries and for patients admitted as emergencies in far from satisfactory condition,

FIG. 8. PPH & SHOCK—NUMBER OF DEATHS IN SIX HOSPITALS

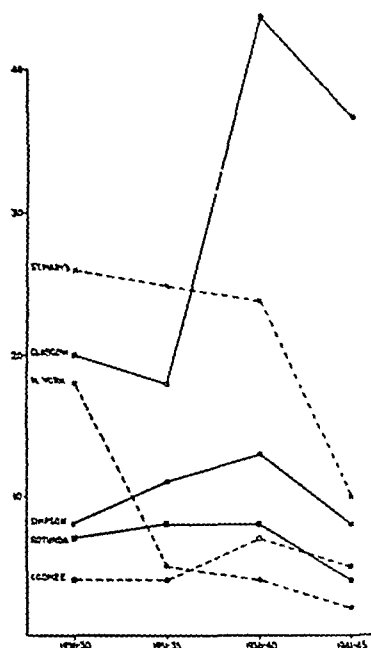
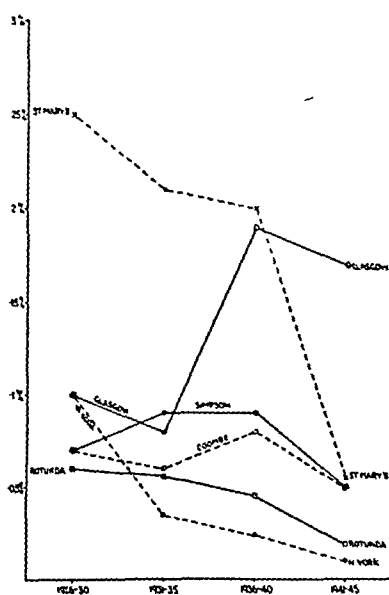


FIG. 8A. PPH & SHOCK—MORTALITY % OF ALL ADMISSIONS AT SIX HOSPITALS



and (3) the large numbers of 10-paras or more who are admitted, whose uteri have lost their power of adequate contraction and retraction. It is possible that the comparatively new method of injection of ergometrine after the delivery of the head may cause a diminution of the number of deaths from this cause, but the treatment is still on its trial in Britain and it is too early yet to be dogmatic regarding its benefits.

It will be seen from Figs. 9 and 9a and Table XII, that the number of deaths from placenta prævia has diminished considerably though the incidence has remained fairly stationary. All mortality rates have decreased and in the Simpson there have been only two deaths from placenta prævia during the last five years and they both occurred in the same year, a mortality percentage 0.9 (against 6.3 in the period 1926-30). These figures have already been discussed in full in this Society by Dr Sturrock, so there remains nothing else for me to contribute

except to draw your attention to his paper and to show you by graphs and tables how the Simpson compares with the other hospitals.

In my opinion the greatly lowered mortality in cases of placenta prævia is due to three main reasons: (1) the adoption of caesarean section for the more dangerous types and the use of Willett's forceps when indicated in place of plugging with the half-breech, (2) the almost routine use of blood transfusion as a prophylactic against the effects of possible dangerous blood loss and also as a replacement for any great loss, and (3) the fact that students have been taught that any case of bleeding in the last three months of pregnancy must have immediate hospitalisation and be examined only by an expert. The high mortality in the earlier years was partly due to examination

FIG. 9. P. PRÆVIA—NUMBER OF DEATHS IN FIVE HOSPITALS

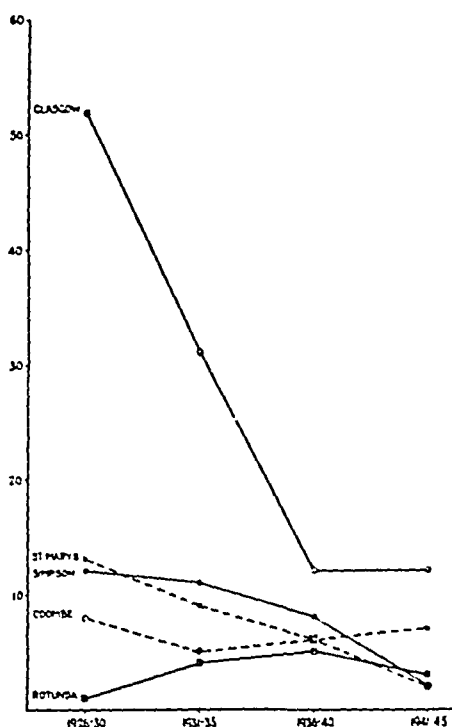
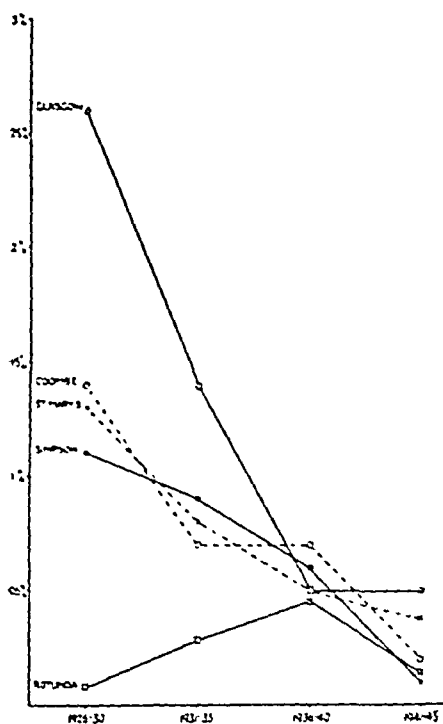


FIG. 10. P. PRÆVIA—MORTALITY % OF ALL ADMISSIONS AT 5 HOSPITALS



being carried out in the patient's house, excessive bleeding being caused, and the patient being sent to hospital in extremis.

In some hospitals, notably in Glasgow, a number of cases are admitted with retained placenta, but these numbers are being diminished by the more frequent use of a "flying squad" of efficient personnel fully equipped with plasma and blood; by this means patients may be adequately treated in their own homes and their condition rendered satisfactory before transport to hospital. This again has been in part due to the better instruction of students so that they have been taught to realise that the safest way to treat these patients is not to move them until shock and blood loss has been dealt with. It is pleasing to record that the Simpson has had no deaths from retained placenta during the last five-year period.

The incidence of accidental hæmorrhage as a cause of maternal death has diminished very considerably, the only hospital in which the mortality is appreciable from 1941-45 being Glasgow, where there were 14 deaths, whereas at the Simpson and at St Mary's only one death was recorded. This improvement is again partly due to better tuition, and partly to a better understanding of the pathology of the condition, and thus to more efficient treatment. Nearly all such cases are now treated expectantly, and caesarean section with or without hysterectomy, which used to be carried out frequently for the concealed variety, is now seldom required. The improvement is also due to the more efficient ante-natal supervision of cases of pre-eclampsia and hypertension. Thus once again a one-time dreaded disease can now be regarded with a degree of equanimity.

FIG. 10 F.F.O.s - NUMBER OF DEATHS  
IN HOSPITAL

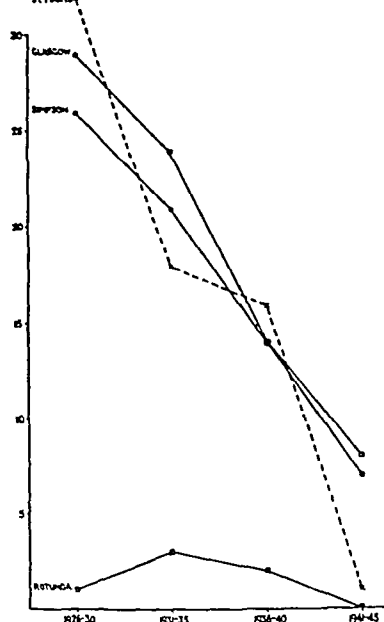
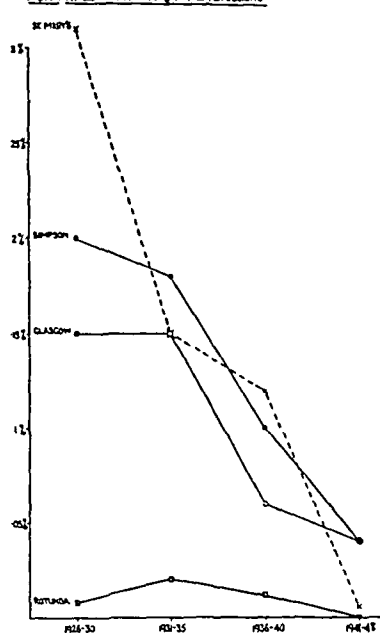


FIG. 10a F.F.O.s - MORTALITY % OF ALL ADMISSIONS

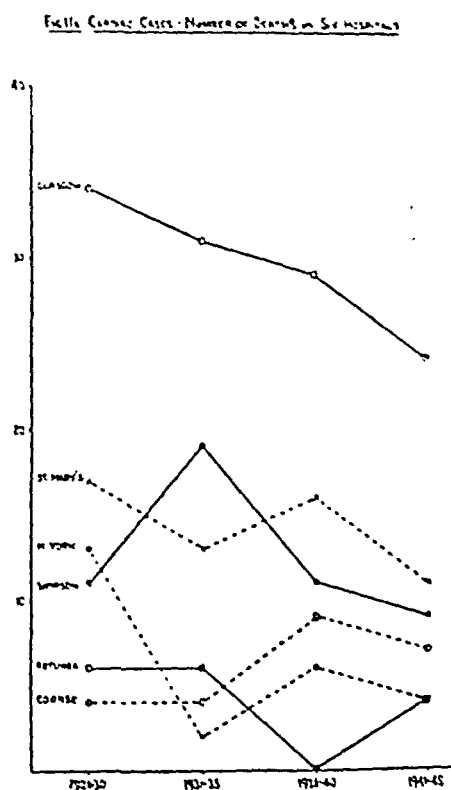
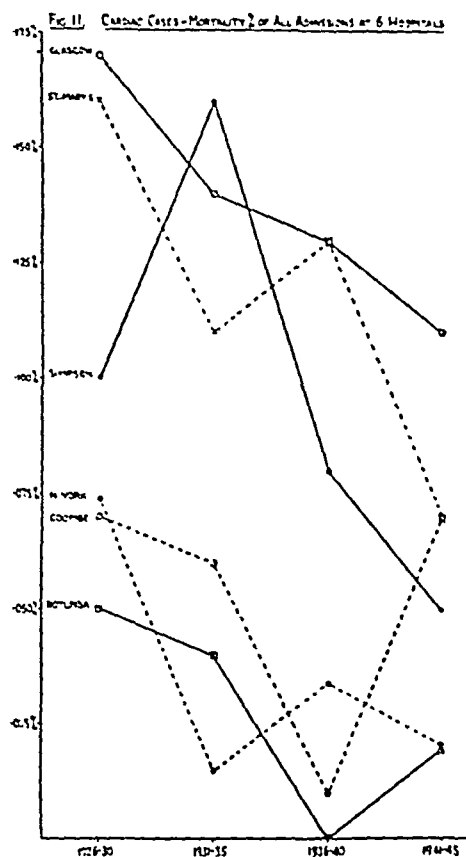


### FAILED FORCEPS OUTSIDE

I would like to refer to another important cause of mortality in hospitals admitting non-booked cases, namely the so-called F.F.O. (failed forceps outside), where the practitioner has tried to deliver with forceps, and, having failed to do so, sends the patient to hospital.

Quite an appreciable number of deaths in Glasgow, St Mary's and at the Simpson have occurred in such cases, especially where there had been gross interference before admission. The causes of death are shock, sepsis, or in a few cases, rupture of the uterus. The improvement achieved in dealing with such cases is illustrated in Figs. 10 and 10a. How has this been accomplished? I would suggest that again it is due to more adequate ante-natal care and improved

methods of treatment in hospital, *e.g.* lower uterine segment caesarean section, blood transfusion, anaesthesia etc., but the main reason is the better instruction of students. It is noted that at the Simpson, though slightly more cases of "failed forceps" were admitted during the period 1941-45 than in the other periods, the mortality rate fell from 36.2 per cent. and 29.2 per cent. in the previous periods, to 9.9 per cent. In this connection it is also to be noted that 11 cases of traumatic rupture of the uterus were treated with only 4 deaths in comparison with 15 cases between 1926-30 with 14 deaths. Thus, though more cases of interference were admitted in the last five years,



they had not been severely mutilated; and forceps had been applied in the majority of cases only once, and that tentatively, whereas in the earlier periods forceps had been applied frequently before the patient was sent to hospital and much trauma had been caused thereby, in many cases being so severe as to have caused rupture of the uterus.

### CARDIAC CASES

From perusal of the Table XIV and Figs. 11 and 11a, it will be seen that the number of deaths from cardiac disease associated with pregnancy has been variable for all the hospitals in the five-yearly periods depicted, but the general trend has been that of improvement. In the Simpson, which has shared in this improvement, the tendency

TABLE XIII—PLACENTA PRÆVIA  
*Results of principal Treatments at The Simpson*

	1926-30.	1931-35.	1936-40.	1941-45.	
	Total	Total.	Total.	Total.	Fetal Deaths.
Plugging with Breech	111	78	38	31	24
Willett's Forceps	2	36	46	47	16
Cæsarean Section	27	22	54	74	16
					Fetal Deaths.
					34
					29
					19

*Combined Statistics for 20 years*

	1926-30.	1931-35.	1936-40.	1941-45.	
	Total Cases.	Total Deaths.	Percentage.	Total Cases.	Percentage.
Plugging with Breech	258	17	6.6	144	72.2
Willett's Forceps	131	3	2.3	100	32
Cæsarean Section	179	3	1.4	155	16.8
					Fetal Deaths.
					104
					32
					26

*After 35th week*

TABLE XIV—CARDIAC CASES (THE SIMPSON)

	1926-30.	1931-35.	1936-40.	1941-45.	
	Total.	Total.	Total.	Total.	Mortality Percentage.
Plugging with Breech	191	181	272	322	9
Willett's Forceps	11	19	11	9	2.8
Cæsarean Section	5.8	10.5	4.0	2.8	
					Mortality Percentage.
					5.9
					2
					14.6
					4
					7.0

*Cæsarean Sections*

	1926-30.	1931-35.	1936-40.	1941-45.	
	Total.	Total.	Total.	Total.	Mortality Percentage.
Plugging with Breech	47	31	36	57	14.6
Willett's Forceps	24.6	17.1	13.2	14.6	4
Cæsarean Section	8.5	19.3	5.9	7.0	
					Mortality Percentage.
					1.9
					3.4
					2.1
					0.82
					1.9

TABLE XV—CÆSAREAN SECTIONS

	1926-30.	1931-35.	1936-40.	1941-45.	
	Total.	Total.	Total.	Total.	Mortality Percentage.
Plugging with Breech	303	296	381	677	1.9
Willett's Forceps	652	1036	1094	1139	3.4
Cæsarean Section	626	715	626	...	2.1
	192	156	203	488	0.82
	54	147	187	209	1.9
					Mortality Percentage.
					1.9
					3.4
					2.1
					0.82
					1.9



has been for treatment to become more conservative, and many cases which would have been treated by caesarean section in earlier years were latterly allowed to have natural labours. This is shown in the percentage of caesarean sections in cardiac patients in the first ten years in comparison with the last ten years. The mortality has not only decreased materially for all cases, but it has also decreased in those cases for whom caesarean section was done and this is possibly due, partly at any rate, to the substitution of local for general anæsthesia for such cases.

### CAESAREAN SECTIONS

There is no doubt as far as the Simpson is concerned that the increased use of caesarean section and the introduction of the lower segment operation, especially in cases which had been previously examined outside, has lowered the maternal mortality. The indications for caesarean section have become more numerous as the years have rolled on and its incidence has become higher as is seen in Table XV which shows an interesting comparison with the other hospitals. This table also shows how the mortality rate has been improved.

### WHAT OF THE FUTURE ?

From the statistics that I have just put before you it will be appreciated that midwifery practice has improved in the last twenty years ; the best results are obtained in the hospitals admitting few if any emergency cases except from their own district cases, which latter are supervised by the hospital ante-natal clinics. There is still room for improvement, especially in the standard of domiciliary midwifery outwith the aegis of the hospital ante-natal clinics, so that potential difficulties are recognised early and their unsuitability for domiciliary care realised ; then only will serious emergency admissions decrease and the few that are not foreseen will arrive in hospital in better trim and without trauma. How can this be achieved ? This is a very important consideration at the present moment when we are approaching a new era in the practice of medicine with the advent of a National Health Service, which includes midwifery. It is the duty of obstetricians therefore to advocate a scheme, which if carried out efficiently and conscientiously will give Britain, despite its large and crowded industrial centres, a chance of producing the lowest mortality, morbidity and infant mortality rates in the world.

My suggestion for future improvement can be summarised under two main headings, though there are many less important considerations to which I have already alluded in this address. The main principles should be : (1) Adequate and efficient ante-natal care for all pregnant women, and (2) Adequate and efficient practical instruction, either before or after qualification, for all practitioners, who desire to practise midwifery.

ADEQUATE AND EFFICIENT ANTE-NATAL CARE FOR ALL  
PREGNANT WOMEN

The importance of efficient ante-natal care can be gauged by noting the disparity between the mortality percentage amongst the booked cases, *i.e.* those who have attended at least two ante-natal clinics (a very low criterion) and the total mortality percentage of all cases admitted, both booked and unbooked, as already remarked upon. The statistics of the New York Lying-in Hospital would seem to afford an excellent example of how efficient ante-natal care for the hospital and surrounding district can lower the mortality to a minimum.

Though ante-natal care has progressed out of all knowledge during the last thirty years it is still far short of being ideal and I would suggest that improvement could be achieved under the following headings:—

(a) *Personnel*.—The responsibility for ante-natal supervision must devolve on those with some extra training in midwifery, which experience alone can make them conversant with its numerous problems and pitfalls. The present undergraduate standard of instruction is only sufficient to permit of practice under supervision. The patient must receive her ante-natal care from the practitioner, who is to attend her at her confinement or at a clinic supervised by the hospital, where she is to be admitted for her confinement.

(b) *Ante-Natal Clinics*.—The large clinics, which are so common in Britain at present owing to the increasing number of ante-natal patients, should be abolished. What clinic can see and examine efficiently 200 or more patients in an afternoon? The clinics should therefore be smaller and more individual, the patient being seen if possible by the same doctor at each visit, so that each case can be followed up satisfactorily and a personal interest taken. This would greatly help the patient's comfiture and confidence, and would be advantageous when slight abnormalities, which might escape notice by a new examiner, made their appearance. No session should be longer than two and a half hours and no individual doctor should undertake the examination of more than 25 cases in that time. Special consultative clinics, personally supervised by a more senior member of the hospital staff should be held for difficult cases and for those for whom the practitioner desires help and advice.

(c) *Accommodation*.—There must be adequate ante-natal in-patient accommodation with sufficient nursing and medical personnel for all patients requiring hospital supervision and treatment such as those suffering from toxæmia, cardiac disability, diabetes, ante-partum hæmorrhage, pyelitis, or mere debility, etc. The first ante-natal bed in the world was provided at the old Simpson Memorial Hospital in 1899 by the late J. W. Ballantyne, but it was not until nearly twenty-five years later that an ante-natal ward came into existence there and it had only 10 beds. When the new pavilion was erected in 1939 it was thought that 25 per cent. of the total beds should be devoted to

ante-natal cases and approximately 30 beds were given over for such cases. This has been found to be entirely insufficient and it would appear that about 40 per cent. of the total beds in a maternity hospital should be devoted to ante-natal cases, the exact proportion depending on the character and working conditions of the population in the area, which the hospital serves. Secondly, sufficient lying-in accommodation must also be provided for all cases regarding the difficulty of whose confinement there is any doubt. This would include all primiparæ and multiparæ who had nine previous confinements, besides patients with slight contraction of the pelvis, with history of previous difficult labours or still-births, etc., besides the more gross abnormalities.

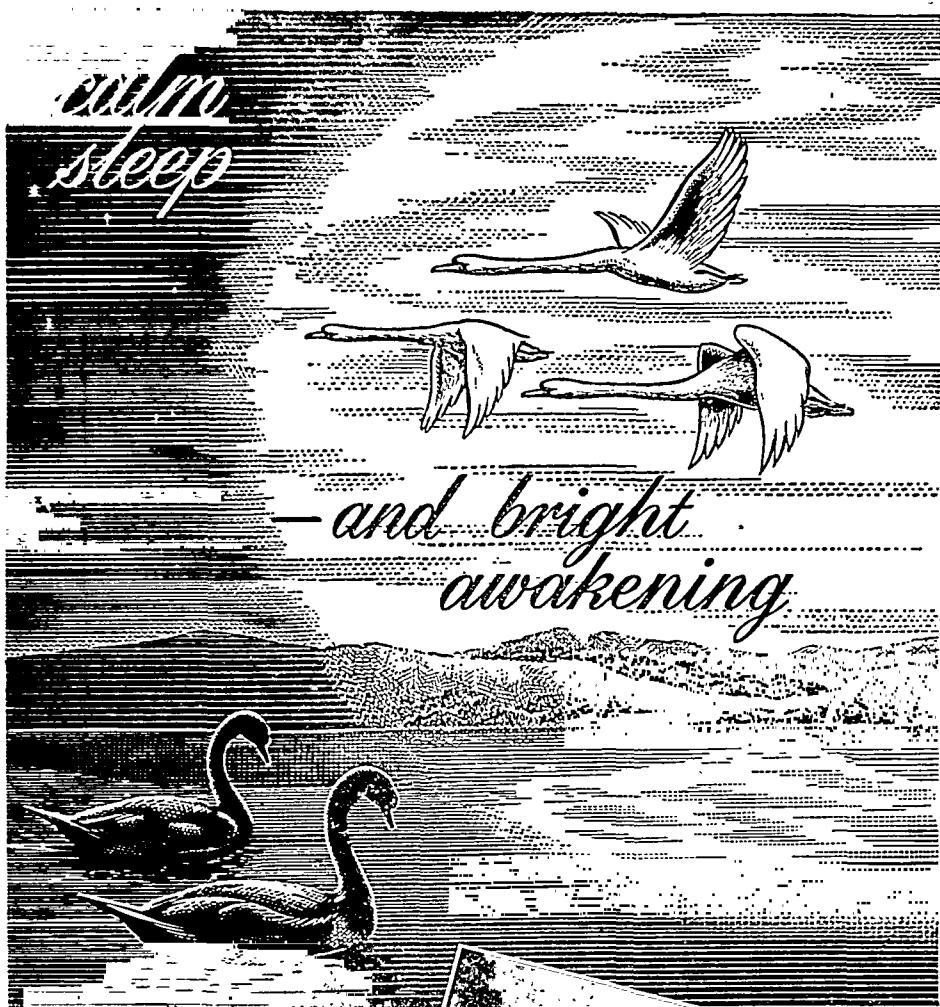
### TEACHING

It has been shown how the improved teaching in midwifery has probably materially affected the maternal mortality and morbidity figures during the last twenty years, but a more thorough practical and clinical training of students or young graduates, who are going to undertake midwifery in their general practice, is still urgently required. Too often still do mothers die or suffer irreparable damage from inadequate ante-natal care, mismanagement of labour or inability to discover that a condition is beyond the practitioner's capabilities; all of which reflect adversely on the extent and efficiency of the present day teaching. The benefits of research in midwifery are jeopardised and the full effect can never be attained if the practitioner has not been efficiently instructed.

I agree wholeheartedly with H. M. Little, who in his presidential address to the Canadian Medical Association in 1924 on the "Progress of Obstetrics in the Preceding Twenty-five Years," stated: "Ante-natal care by itself is hopeless without some improvement in the teaching and practice of obstetrics. The most recent graduate is no more capable of undertaking any but the simplest midwifery cases than he is to practise abdominal surgery." It may be of passing interest to note that both Professor Johnstone and myself made very similar statements to this Society in 1935.

Undergraduate training in midwifery in Britain has advanced greatly in the last twenty years, but the average graduate is still allowed to go into general practice badly equipped in practical experience though his theoretical knowledge may be satisfactory.

The question of instruction is of paramount importance at the present time when, under the English National Health Service Act, midwives in difficulty are only allowed to call in doctors who are "suitably qualified," and it would seem that the Scottish Act has lost a great chance of improving midwifery in Scotland also, by deleting before its second reading, the adoption of a similar qualification for the practitioner who undertakes midwifery practice under the 1937 Maternity Act, which is to be incorporated in the new Act. There



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is no doubt that midwifery in general should be carried out by general practitioners and midwives and it certainly has never been my contention that it should be taken out of the general practitioners' province. Practitioners have, however, taken great exception to the wording "suitably qualified" and, having managed to get the words deleted from the Scottish Act, are still endeavouring to secure deletion in the English Act. This is extremely unfortunate for the efficiency of general midwifery practice in the country, and if it could be stated to the practitioners that anyone who had practised midwifery in general practice for five years would be recognised as suitably qualified, and that for the newly qualified all that would be required would be some extra intensive training in midwifery and not any necessity of securing a higher diploma, such as the D.(Obst.)R.C.O.G., then it might be hoped that the antagonism shown at the present time might be dissolved and a harmonious scheme evolved which would greatly improve the standard of midwifery for the country.

If such a scheme were acceptable, then it would be the duty of the teachers of midwifery to supply an intensive course for those who wanted to practise midwifery. It has been stated that further practical training for the undergraduate is impossible owing to lack of patients and teachers; this is probably the case if teaching is carried out according to the present curriculum, but for the time remaining I would ask your indulgence to be permitted to suggest a scheme of training which in my opinion would be practicable and would provide sufficient "suitably qualified" practitioners to carry out general midwifery in this country in a satisfactory manner.

In the first place it is probably correct to state that only a proportion of students who qualify want to practise midwifery; many practitioners at present in general practice only do so unwillingly as it is expected of them by their patients. Under the New Health Services Act, when midwifery practice will not be an essential for the practitioner, there will probably be a larger proportion of doctors than previously, who will not wish to undertake any midwifery practice. Many in the past had no interest in midwifery and looked upon their midwifery practice as an essential nuisance; it is not unlikely that in the practice of these practitioners midwifery was hurried and slipshod and that maternal and foetal mortality and morbidity had suffered thereby.

I would suggest therefore that all students should do a course on midwifery, gynaecology and the care of the new-born during their curriculum and that this course should include lectures and clinics. The course would differ from that given at present in that it would deal chiefly with normal midwifery, including anatomy and physiology; the abnormal would only be touched upon and would not be gone into in detail, excepting the pathology of pregnancy, which would be taught more thoroughly especially in regard to those medical conditions associated with pregnancy that come into the general practitioner's province. Clinical work would augment this scheme and would be

devoted chiefly to ante-natal care and pathology, normal labour and the normal puerperium, including minor deviations from the normal. During this time the student would personally conduct five cases in labour in hospital under supervision, and would follow up these cases during the puerperium. Instruction on breast and bottle feeding should be included as well as lectures and clinics on the new-born and its care, with some reference to the more common diseases that may occur in the first few weeks of life. Attendance at child welfare clinics would also be required. Gynæcology should be taught similarly to other specialties, the more common diseases being discussed fully, and the student should be taught how to make a vaginal examination so as to be able to recognise the abnormal from the normal. He should be shown clinically the more common gynæcological conditions but there would be no necessity to teach him advanced diagnosis or major operative treatment; he should, however, be instructed in the treatment of such gynæcological complaints (vaginal discharge, etc.), as are responsive to non-operative measures. There would be no necessity for these students to be in residence in a maternity hospital nor would they be required to attend district cases, so more accommodation and cases would be available for others. These students would be required to take an examination on the curriculum which they had been taught, in the final examination. This would relieve the teachers' burden as lectures and clinics would not be so numerous as at present.

After passing the final examination, the General Medical Council has recommended that a further year should be spent in residence in a hospital in order that the student may do more advanced clinical work before a degree is conferred upon him. I would suggest that during this year all students who wished to practise midwifery later might spend three months doing an intensive course during which they would be required to live in the precincts of a maternity hospital and would receive a further course of lectures on the abnormal midwifery which can be suitably undertaken by the general practitioner. They would be divided into sections of not more than ten to attend clinics in abnormal midwifery and be instructed individually in practical midwifery, such as the application of forceps, rotation of the head in occipito-posterior positions, episiotomy, perineal suture, delivery of abnormal presentations such as breech and face, and the diagnosis of abnormal conditions such as placenta prævia, contracted pelvis, etc.; they would also be taught how to recognise abnormalities, which were outside the province of the general practitioner, and how to realise this fact. They would attend ante-natal and post-natal clinics and would get abundant opportunity to examine cases themselves. They would be required to attend ten more cases for their confinements and puerperia, and the majority of these cases should be on the district. In the main, clinics should be taken by the more senior obstetricians as there is probably no subject in which experience is of more importance in teaching than midwifery, but tutorials would also be a feature of

the course and these would be carried out by the more junior specialists and the clinical tutors. The students would also get further instruction on the new-born and child welfare, at which clinics they would take an active part. A little more advanced gynæcology might also be included especially in association with post-natal care and its sequelæ.

The number of students who, under such a scheme, might wish to make themselves "suitably qualified" is difficult to predict, but would probably be not more than 60 per cent. of any one year; if, however, the yearly number of students was too large to accommodate them in the main teaching hospital for a university, then other maternity hospitals could be used with advantage. At the termination of the course there should be a further examination, which would be both clinical and oral, and on passing this examination it might be possible for the university concerned to confer another degree such as B.A.O., or B.Obst. which would show that the newly-fledged graduate had made himself "suitably qualified" in midwifery. These courses would also be open to any graduate, who at a later date, not having already done so, desired to make himself "suitably qualified" and he would receive the extra degree after passing the examination. There should also be arranged general practitioners' refresher courses in midwifery, each lasting seven to ten days, which the "suitably qualified" practitioner would attend once every five years so as to receive instruction on the latest advances and to bring his midwifery up to date.

Surely the general practitioner could not object to a scheme such as this, which I consider would be possible to carry out with the clinical material that is at present available in this country, and with only a slight increase in the teaching staffs; by so doing I consider that the universities could supply a sufficient number of general practitioners capable of practising midwifery efficiently and by their skill the standard of midwifery in this country would be raised to a height that has never previously been attained.



# INFANTILE CEREBRAL HEMIPLEGIA—CLINICAL FEATURES AND PATHOLOGICAL ANATOMY

By ROY MACKENZIE STEWART, M.D., F.R.C.P. (Edin. and Lond.)

MR PRESIDENT, Fellows, Ladies and Gentlemen, in thanking you for the honour the College has done me by inviting me to deliver the Morison lecture for 1947 I must also betray to you my consciousness of how difficult it will be for me to uphold the high standards established by my distinguished predecessors. For in presenting to you observations on certain clinical and pathological aspects of infantile cerebral hemiplegia I am well aware of the small extent to which anything I say can claim to be original.

The clinical importance of this subject is beyond doubt and its literature is already voluminous, but despite this we still lack a clear concept of many aspects of its etiology and with this lack in view it seemed to me that the survey of another series of cases, all of which I have observed personally, might not be altogether redundant.

Whereas the early studies of Freud (1897), Osler (1889), Sachs, Peterson (1890), and others were based on cases seen in infancy and childhood, mine deal almost exclusively with the features of infantile hemiplegia as portrayed in adult life when the condition has become stabilised. Such material, if not very fruitful for clinical observation, has at least the merit of providing a wealth of material for pathological investigation.

The 112 cases included in this study were all patients in an institution for mental defectives, and consequently they represent a narrow selected group handicapped by marked mental retardation. Fifty of them were males, and 62 females. Right hemiplegia occurred in 61 and left hemiplegia in 51. (Table I shows the ages at onset.)

TABLE I  
*Ages at Onset*

	Male.	Female.
Congenital . . . . .	15	21
During 1st year . . . . .	19	22
2nd year . . . . .	10	7
3rd year . . . . .	1	4
4th year . . . . .	1	2
5th year . . . . .	3	3
Unascertained . . . . .	1	3
	<hr/> 50	<hr/> 62

In 102 cases, or 91 per cent., the hemiplegia was either congenital or occurred during the first three years of life.

Being the Morison Lecture delivered 28th November 1947 in the Royal College of Physicians, Edinburgh.

It is customary to recognise three groups for purposes of classification: those of prenatal origin, those due to injury sustained at birth, and those acquired in the first few years of life. Yet this distinction can seldom be made with certainty, since the signs of paralysis determined before birth are often tardy in their appearance, and indeed, may not become obvious until weeks or months have elapsed.\* Moreover, in early infancy, not spasticity, but weakness and hypotonia are the indications of hemiplegia, and consequently its cerebral nature may escape recognition until the age when the child attempts to walk. Thus many a congenital hemiplegia is wrongly labelled "acquired." With regard to etiological factors, those which appear in Table II follow familiar lines.

TABLE II

*Etiological Factors**Congenital hemiplegia. 50 cases—*

Ill health of mother during pregnancy . . . . .	10
Injury to mother by fall during pregnancy . . . . .	2
Difficult or abnormal labour . . . . .	26
Cerebral angioma with facial naevus . . . . .	2
Unascertained . . . . .	10

*Acquired hemiplegia. 62 cases—*

Injury to head . . . . .	4
Tuberous sclerosis . . . . .	2
Measles . . . . .	1
Scarlet fever . . . . .	1
Whooping cough . . . . .	3
Encephalitis . . . . .	7
Meningitis . . . . .	6
Vaccinia . . . . .	3
Congenital Syphilis . . . . .	9
Unascertained . . . . .	26

Many writers have insisted on the association of paralysis with difficult or abnormal labour. Ford, Crowthers and Putnam (1927) obtained a history of abnormal labour in 70 per cent. of monoplegias and hemiplegias, and in a statistical analysis of 86 patients in whom the diagnosis of congenital cerebral palsy was made Yannet (1944) obtained a history of abnormal labour in about 25 per cent. of all the cases. The greatest incidence was found in the mothers of infants with hemiplegia; almost 50 per cent. of the deliveries were described

\* Norman (1947) has convincingly demonstrated that diseased conditions occurring in intrauterine life can cause a hemiplegia whose appearance is delayed until well on in the first years of life. His patient was one of twins, and from the clinical history it would appear that the onset of hemiplegia was delayed certainly until after the age of eighteen months and probably until the age of three years. The pathological findings, which were diverse, included a stunted left hemisphere with dilatation of the lateral ventricle, narrow and tortuous gyri, état marbré in the caudate nucleus, and, most important of all, paraventricular softening of the central white matter in the left frontal lobe. The latter finding may be regarded as pathognomonic of the terminal vein lesions of birth injury.

as abnormally difficult. In the present series a history of a normal labour was obtained in 26 cases, or 23 per cent., a figure sufficiently large to uphold the claim that birth injury plays an important part in the etiology of the asymmetrical palsies of childhood.

A closer analysis of the cases which I have included under the heading "abnormal labour" shows the following categories.

TABLE III

*Analysis of 26 Cases with History of Abnormal Labour*

Precipitate delivery . . . . .	1
Prematurity . . . . .	4
Breech presentation . . . . .	1
Asphyxia . . . . .	1
Instrumental birth . . . . .	5
Injury to foetal head . . . . .	6
Convulsions in first few days of life . . . . .	3
Unascertained . . . . .	5

Four of the six cases with a definite history of injury to the head during delivery were followed to autopsy, and in all of them the lesions were found to be those usually thought characteristic of birth injury.

Osler (1889) commented on the vigorous healthy-looking condition of the mothers with hemiplegic infants and of the absence of nervous disease in the parents of such children. Such has not been my experience: for under the category "congenital hemiplegia" a history of maternal ill-health during pregnancy was obtained in ten instances. Of these, perhaps the most interesting was that of a woman who contracted typhoid fever in the fourth month of pregnancy. Her child was born with a left-sided hemiplegia, and in adolescence he showed signs of dystrophia adiposogenitalis. Though hemiplegia is known to be an occasional complication of typhoid fever acquired in childhood, this association with maternal typhoid must be rare; and the only relevant report which I have been able to find is a reference by Osler to a cavity which he found in the brain of a foetus whose mother died from typhoid fever in the sixth month of pregnancy.

According to James Taylor (1905), in two-thirds of all cases of infantile hemiplegia the paralysis is ushered in by convulsions. Sachs (1925) claimed that in certain cases convulsions are the cause of the paralysis and not merely part of the symptomatology, but no direct evidence for such a view has ever been produced.

The connection of infantile hemiplegia with congenital syphilis is usually held to be remote, and it has been stated that when present the paralysis dates from birth. The presence of histories of congenital syphilis in nine cases in my series is not altogether in accord with such a view. Furthermore, in six of them the hemiplegia was acquired in the second or third year of life, and only in one, that of an idiot, blind, deaf and dumb, was the paralysis of congenital origin. As a rule the stigmata of congenital syphilis are well marked.

One may perhaps question the propriety of placing tuberous sclerosis in the etiological table of acquired hemiplegia; but I have done so because in both instances the hemiplegia did not occur until the second or third year of postnatal life.

In general, the residual physical signs of hemiplegia do not differ materially from those which were displayed in early life. Arm, leg and face are affected in diminishing order of severity. The typical picture of the upper limb is one of adduction with the upper arm held in close juxtaposition to the trunk, flexion at elbow, the forearm semi-pronated, flexion and ulnar deviation at wrist, thumb flexed into palm with fingers usually embracing it. The paralysis is progressively more evident towards the periphery of the limb and contractures are seldom absent. As a rule the arm is of little value for the ordinary purposes of life. Not every patient, however, shows so much disability, for full or nearly full extension at the elbow is by no means uncommon.

In the hemiplegia acquired in adult life associated movements are uncommon. In the infantile variety they are both frequent and marked. Thus, when patient is asked to close the normal hand or to button or unbutton his clothes, the paralysed hand at once imitates these movements. In two of my patients forcible closure of the jaw was sufficient to evoke a general flexion of the paralysed upper limb.

The lower limb almost invariably retains more power than the arm and is most paralysed in the peripheral segments. The usual picture is one of inward rotation at the hip and very slight flexion at the knee. The foot is usually in the attitude of pes equinus or pes equino-varus. Though many patients exhibit the gait of the adult hemiplegia some succeed in acquiring an almost normal gait. Others, severely handicapped by shortening of the leg, progress by hopping. Two of my patients showed the rare condition of flexor contracture of the hemiplegic leg. They presented no evidence of arthropathy or hyperæsthesia on the affected side. It is particularly in the lower limb that the so-called trophic changes are seen. Of these a persistent solid œdema is the commonest. In the present series the 5 patients with this condition were all of the female sex.

Osler claimed that rapid and complete disappearance of the facial paralysis is the rule. That permanent involvement of the face is not nearly so infrequent as has been thought is shown by the presence of some degree of paralysis in 90 of the 112 patients in my series.

Elevation of the brows and simultaneous closure of both eyes is accomplished without difficulty, but movements of the lower half of the face are obviously impaired. This can be readily demonstrated by asking the patient to balloon out the cheek or to show his teeth. Minor degrees of facial weakness may only be evident by the patient's failure to close the eye on the affected side.

Facial paresis also shows itself in emotional movements such as those of smiling or laughing. Twenty-four patients showed equal emotional movement on the two sides; in 14 it was diminished and

in 6 the movements in smiling appeared exaggerated on the paresed side.

Deviation of the protruded tongue to the paralysed side was noted in 11 patients, and squint, external or internal, in 19 instances. The reflexes are those of pyramidal disease, subject to the variations which distinguish this type of hemiplegia. Thus ankle clonus on the affected side is uncommon: it was seen in only 6 patients. Preservation of the homolateral abdominal reflex is another distinguishing feature. In 97 the reflex was present on both sides, in 15 it was absent on the paralysed side.

Involuntary movements appeared infrequently; choreoathetosis was present in 9 and marked homolateral tremor in 4 patients.

As in the adult form, shortly after the onset, flaccidity of the child's paralysed limbs gives place to spasticity; and this is followed in its turn by varying degrees of atrophy and contracture. It is important to stress that in infancy the hemiatrophy is of a dual nature: partly it is of muscular origin, but to an equal, and perhaps greater extent, it is the expression of an arrest of development on the paralysed side. In the child whose bones are plastic a paralysis which in an adult causes only wasting may produce a very striking degree of asymmetry and deformity. To a large extent the degree of retarded development that will result finally depends upon the age at which the disease begins; the younger the child the more marked will be the inequality of the two halves of the body when the period of growth ends. Stunting of growth may implicate the whole of the affected side, but its effects are particularly manifest in the head and upper limb. Not only is the cranium smaller in the region of the affected hemisphere, but in nearly every case the whole head is much below the average in size. In my series only 3 patients attained the normal head circumference of 56 cm., though extreme degrees of smallness, such as one so often sees in diplegia, were not found.

X-ray examination of the skull gives a fairly uniform picture. Adaptation of the brain case to the loss of cerebral substance is indicated by thickening of the cranial vault, strictly limited to the side of the lesion, enlargement of the homolateral frontal and ethmoidal sinuses and of the air cells of the petrous pyramid of the temporal bone. In addition, marked asymmetry of the medial cranial fossa is not unusual, and when crossed atrophy of the cerebellum exists the posterior fossa may also be implicated. Occasionally, not only the cranial vault but also the scalp participates in the localised thickening and in one patient I found a redundancy and corrugation, such as one sees in microcephaly, but in this case strictly limited to the side of the cerebral defect. In some cases, particularly when porencephaly is suspected, it may be possible to detect localised flattening of the cranial bones overlying the damaged region of the brain.

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on the damaged side is not fully understood. Casamajor and Laidlaw (1939) state that room for the growing brain is made by an increase of bone on the outer surface, with a disappearance of bone on the inner, and that when the brain does not grow, or grows more slowly on one side than the other, the process of bone disappearance on the inner side does not take place. Consequently on the affected side the skull becomes thicker. It seems to me that implicit in this explanation is the assumption that each half of the brain controls the growth of the corresponding half of the cranial vault overlying it. For this I can find no established authority in any textbook.

The introduction of encephalography and ventriculography has materially aided diagnosis, for it is now possible to recognise the site and probable nature of certain types of cerebral lesion during life. Apart from the rare instances of gross loss of cerebral substance, such as is found in porencephaly, there is a fairly uniform encephalographic picture common to the majority of cases of infantile hemiplegia. Together with the increased thickness of skull and enlargement of air sinuses on the affected side, one sees an exaggeration of the cortical markings, an enlargement of the lateral ventricle or some part of it, a less frequent dilatation of the third ventricle, and, in a few instances, a displacement of the ventricular system towards the side of the lesion. Through the courtesy of Mr Wylie McKissock I was able to submit 64 patients to X-ray examination and lumbar encephalography.

In 9 cases the cranium appeared symmetrical, and in 29 there was evidence of cranial hemiatrophy. In two instances the encephalographic appearances were those of porencephaly. Various degrees of unilateral ventricular dilatation with an associated cortical atrophy were observed in 56 cases, and in 10 there was a displacement of the entire ventricular system towards the affected side. According to Crowthers and Wyatt (1941) movement of the contralateral ventricle towards the side of the brain atrophy is determined, not by traction from the side of the atrophy, but by the growth of the unaffected hemisphere. If this hypothesis is correct displacement is a favourable sign since it indicates that at least one hemisphere has retained the normal power of growth. Consequently, in spite of the deviation, the degree of mental defect need not be severe: and this was the case in my 10 cases, 7 of whom were feeble minded.

Occasionally not only the cranium but also the whole face shares in the arrest of growth, the resulting asymmetry being evident in the upper as well as in the lower half, sometimes even when no loss of power can be detected in the facial muscles.

In adult cases the presence of some degree of scoliosis makes accurate measurement of the two halves of the chest and the trunk difficult, but there is no doubt that in the majority of old standing cases this part of the body also shares in the undergrowth; but only when the cerebral lesion is extensive is the asymmetry of the trunk marked.

But it is especially in the upper limb that stunting of growth is



most striking. The shortening may amount to several inches, and the number of cases in which the arms are of equal length is very small indeed. As a rule, the more wasted the arm the greater the severity of contracture at elbow, wrist and fingers. On the other hand, the degree of arrested development seems to bear no relation to the amount of paralysis present, a most marked undergrowth being compatible with a minor degree of paralysis. Although upper arm and forearm share in the reduction, it is particularly the hand which retains the puniness of early life, and with the small hand there is often associated a marked degree of hypotonia, even when proximal segments of the limb are extremely spastic. Sometimes the whole hand is flaccid and flail-like, or the hypotonia may be limited to the thumb or to one or more of the fingers. In the experience of Ford (1944), flaccidity in the distal segments of the limb is relatively more frequent in congenital hemiplegia than among those cases occurring later in life. On investigating this point I found no great difference: 14 congenital and 19 acquired cases showed marked hypotonia of the digits. In one case hypotonia could be demonstrated in the foot.

In infantile hemiplegia the leg is usually less affected than in the paralysis of adult life and stunting of growth, particularly of longitudinal growth, is seldom severe, even when the homolateral upper limb is dwarfed to a marked degree.

Occasionally disturbance of growth extends to glandular structures. The mamma and the testicle may be much smaller on the affected side. None of my female patients exhibited asymmetry of the breasts, but an atrophied testicle was found in 6 males. On the other hand, there may be found in rare instances not hypoplasia, but hypertrophy upon the paralysed side. Usually it is the subcutaneous tissues which are involved, the affected leg showing a fat hypertrophy similar to that seen in a limb paralysed from an attack of anterior poliomyelitis. Then again, structures whose growth is normally continuous throughout life are involved; the hair and nails of the paralysed side grow more slowly than on the normal limbs.

Why disturbance of growth in infantile hemiplegia should be so marked in some cases and not in others has long been a subject for discussion. Atrophy from disuse, loss of motor control over anterior horn cells, implication of the autonomic nervous system, and disorder of the vasomotor mechanism have all been put forward at one time or another as possible explanations. This problem has recently engaged the attention of Penfield and Robertson (1943). Their material comprised a number of epileptic patients with varying degrees of bodily asymmetry, some with paralysis, and some without, and in all of whom there were local cerebral lesions dating from the age of two years or earlier. At operation, the use of local anæsthesia allowed the position of the Rolandic cortex to be defined by electric stimulation, and thus the relation of the lesion to this motor area was adequately established in each case. Included for purposes of control were a

number of epileptics with the cerebral lesions of childhood, but without somatic asymmetry. It was found that comparative smallness of the contralateral part of the body was regularly associated with infantile lesions of the postcentral cortex. It was noted, too, that the degree of diffuse somatic atrophy is usually greater when it results from a large lesion of the central region of the hemisphere. Whether this added degree of atrophy is due to disuse or to involvement of subcortical structures they were unable to say. In the majority of cases the area of cortex involved appeared to correspond accurately with the region of somatic smallness. And from these considerations the conclusion seemed justified that the postcentral area has an important influence on growth on the opposite side of the body. In the pathological material at my disposal the lesions were all too diffuse to permit of any conclusions regarding this association.

As the postcentral gyrus is part of the so-called sensory cortex, concerned essentially with spatial and discriminative elements of sensation, a lesion in this neighbourhood should determine disturbance of sensation, and although it is often stated in current textbooks that in its residual form the hemiplegia of infancy is purely motor in type, there is no doubt that sensory loss may occur. Sensory impairment was present in 4 cases of long-standing hemiplegia investigated by Penfield and Robertson, and, after excluding unsuitable subjects, I was able to find 16 in whom it was possible to demonstrate on repeated examination the presence of astereognosis, impairment of two-point discrimination, and loss of vibration and position sense in the fingers.

So far I have spoken only of arrested physical growth, but of no less importance is the serious effect of the brain lesion on the growth of the intellectual faculties. Mental deficiency in some degree is the distressing sequence in a large proportion of cases. Estimates of its incidence vary widely, according to the source of the material. McIntire (1938) states that of persons in the general population with infantile cerebral palsy about 25 per cent. are mentally defective. In their series of infantile hemiplegias Sachs and Peterson (1890) found an incidence of 52 per cent., while Silverskiöld (1924) claimed that only 18 per cent. were thus afflicted. The degree of defect varies from a scarcely noticeable dullness to profound idiocy. It may be expected that the effects of damage limited to one half of the brain will have a less disturbing influence upon the mental development than when the disease affects both halves, and that this is so is indicated by a comparison of the intelligence quotients of my 112 infantile hemiplegics with those of an equal number of diplegics (Fig. 1). Of the hemiplegics, 14 were idiots, whereas no less than 58 diplegics were of this grade. While there is no doubt that the degree of mental defect has a direct relationship to the position and area of the diseased cerebral tissue, the age of the subject at the onset of the hemiplegia is also an important factor. The earlier in life the hemiplegia is sustained, the more serious will be its effects on the growth of intelli-

gence; and the nearer the age approximates to the period when the brain has ceased its development—about the seventh year—the less the interference with intelligence. Hence, the subjects of congenital hemiplegia are usually either idiots or low-grade imbeciles. Possibly too, genetic influences play some part in determining the presence of mental defect in this form of paralysis, for I have not found the immunity from morbid inheritance to which some writers refer.

A history of epilepsy or insanity in one of other parent was obtained in 27 instances, or 24 per cent. In the families of my patients there

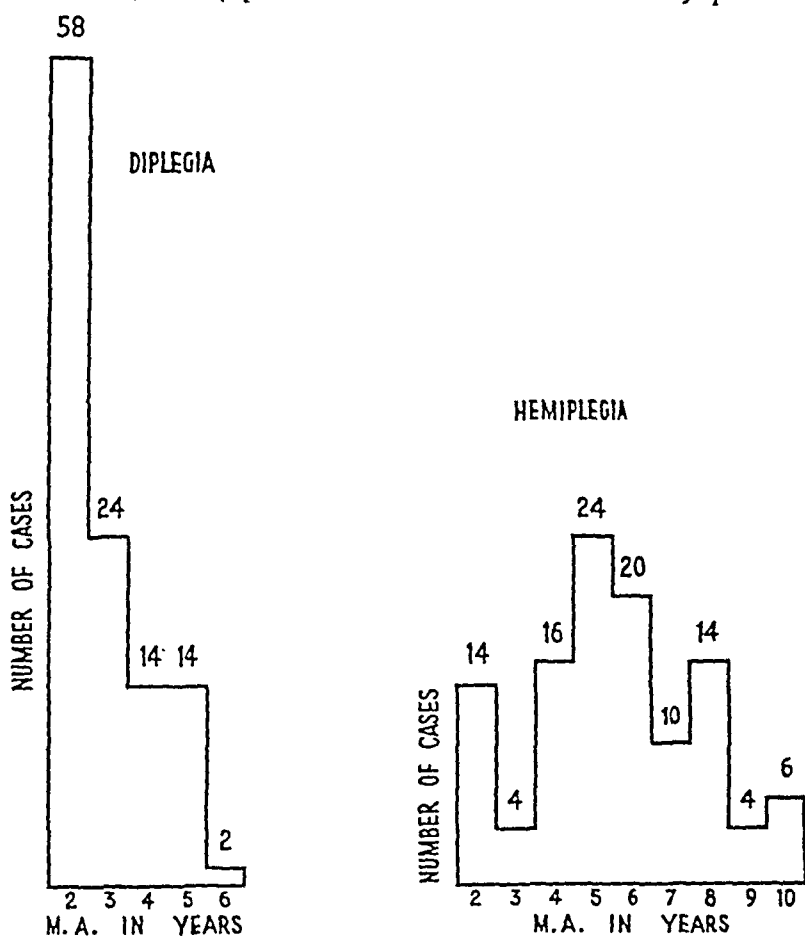


FIG. 1.—Comparison of mental ages of 112 cases of cerebral diplegia with those of 112 cases of infantile hemiplegia.

were 420 siblings not affected by paralysis, of whom 17 were mentally defective. Probably this number is an understatement, as parents tend to gloss over the presence of mental defect in their families. But if we accept this figure as correct, it indicates a rate of 4 per cent. mentally defective. As the estimated incidence of amentia in the general population is about 1 per cent., there is thus a significant increase of mental deficiency in the non-paralysed siblings. On the other hand, the presence of organic nervous disease in other members of the family is rare. Yannet (1944) found a recurrence of cerebral palsy in another later born sibling in 6.5 per cent. of the families, but

there were no instances of familial hemiplegia, and I believe its occurrence has never been reported. I have, however, notes of a family in which the elder child acquired hemiplegia and the younger cerebral diplegia.

If, as we have seen, paralysis limited to one half of the body has less serious consequences on mental development than when both sides are involved, in respect of the incidence of epilepsy the exact opposite is the case. Fits are far more common in hemiplegic subjects than they are in the diplegias and paraplegias of infancy. According to Sachs (1925) about one-half of all cases of infantile hemiplegia are subject to recurring fits, while in diplegia the incidence is about one-third of cases. Of the 112 hemiplegic patients in my series, 79 or 75 per cent. had been subject to fits at one time or another. While of 112 diplegics (of rather lower age groups), 44 or 39 per cent., were epileptic. In the series presented by Yannett (1944) 68 per cent. suffered from severe and persistent convulsions. Though the fits usually start on the paralysed side in established cases, general and not localised epilepsy is the rule. Its development is not necessarily proportionate to the severity of the paralysis; the latter may be slight, and the former severe. The date when the attacks begin after the onset of hemiplegia varies considerably, and may be delayed until long after the onset of the paralysis. But once established, the fits are persistent, and though often mild, usually continue for the rest of the patient's life. An aura is usually present, but an initial cry is rare, and consciousness may be retained if the fit is confined to one side.

A word may be said regarding disturbance of speech. It is well known that in children who have not yet begun to talk, or in whom the speech function is not fully developed, cerebral lesions usually result in complete loss of speech, and not fractional loss as in older children. As a rule, the aphasia which develops in subjects who have learnt to talk resembles the motor variety of adult life, but there is this important difference: whereas in adults aphasia is almost invariably associated with paralysis on the right side, except in left-handed individuals, in children it occurs almost as frequently on the left side as on the right. Out of 324 cases of aphasia in children reported by Taylor (1905) 200 were instances of right hemiplegia and 124 were cases of left hemiplegia. In a smaller series, Sachs (1925) reported 10 aphasic children with right and 7 with left hemiplegia. Figures such as these indicate the plasticity of the growing child's neural mechanism. As we grow older we become more and more left-brained.

Another distinguishing feature is the transitory character of the speech disturbance. Except in the rare instances in which bilateral lesions of the speech centres exist, the power of speech soon returns, and is usually completely restored within a year. In the present series there were 2 idiots completely unable to speak, and in 8 other cases a marked degree of dysarthria was present, but in no single were the true psychological components of aphasia found.

I may allude in passing to the interesting condition termed "mirror-

writing," in which script is written in an opposite direction to the normal, the individual letters also being reversed. The phenomenon is not uncommon in mentally defective children who present no physical disability, but its incidence is probably larger when, in addition, there is paralysis. Out of 79 hemiplegics reported by Fraenkel (1908), 21 showed a left-sided hemiplegia, and of these three wrote mirror-writing with the paretic hand. Of the remaining 58 cases with right-sided paralysis, 21 wrote in the mirror fashion with their left hands.

Ten of my patients, all examples of right-sided hemiplegia, showed this faculty. The small incidence is probably related to the relatively large number who were illiterate. Of these the most interesting was that of a feeble-minded woman, aged 29, whose right-sided hemiplegia dated from the tenth month. With her left hand she could write her name with equal facility in three forms: in the normal left to right way, mirror-wise, and in inverted fashion. She exhibited neither aphasia nor apraxia, but claimed that pictures in magazines were more readily understood when she held them before her upside-down. Her ability to write was limited to her own name and to the letters of the alphabet. In reading, individual letters of the alphabet were frequently mistaken for each other, and she had considerable difficulty with words of more than one syllable.

It would take too long to review all the numerous theories which have been put forward to explain mirror-writing, but in relation to its occurrence in congenital hemiplegia the "motor" hypothesis of Erlenmeyer (1879) seems most acceptable. This may be summarised by the statement that the most natural movements for one hand are the mirrored replica of those of the opposite hand, abductive or centrifugal movements being the easiest, most co-ordinate and best controlled movements. For the appearance of inverted writing some other theory is necessary. Critchley (1928) suggests that defective visual perception is the chief factor responsible.

### MORBID ANATOMY

I now turn to a consideration of the morbid conditions underlying this type of paralysis (Tables IV, V and VI), and since in this series we are dealing with end results which cannot be expected to throw

TABLE IV

#### *Infantile Hemiplegia: Morbid Anatomy*

<i>Congenital</i>		<i>Acquired</i>	
Porencephaly . . . . .	2	Internal hydrocephalus . . . . .	3
Pseudoporencephaly . . . . .	3	Sinus thrombosis . . . . .	1
Hemiatrophy . . . . .	3	Hemiatrophy . . . . .	4
Atrophic lobar sclerosis . . . . .	9	Tuberous sclerosis . . . . .	2
	—	Atrophic lobar sclerosis . . . . .	3
	17	Sclerosis of white matter . . . . .	1
	—	Unilateral hypoplasia . . . . .	3
			—

much light on the initial pathological process, it would serve no useful purpose to enter into a detailed discussion of all the anatomical changes that may be found.

TABLE V  
*Infantile Hemiplegia: Congenital. Brain Weights \**

	Side of Paralysis.	Duration (years).	Morbidity Anatomy.	Total Brain wt. in gm.	Cerebral Hemisphere		Cerebellum and Brain Stem.	Crossed Atrophy of Cerebellum.	Remarks.
					Right.	Left.			
1	Left	18	Porencephaly	751			?	—	...
2	"	30	Porencephaly and microcephaly	768	?	374	172	+	...
3	"	32	Pseudoporencephaly	1033	222	521	145	—	...
4	"	68	Lobar sclerosis and hemi-atrophy	649	367	380	95	+	...
5	Right	57	Lobar sclerosis	862	174	310	112	+	...
6	"	57	"	993	440	408	130	—	...
7	"	36	"	1130	455	470	165	—	...
8	Left	22	"	804	495	377	115	+	...
9	Right	49	Lobar sclerosis and microcephaly	658	312	235	138	—	...
10	Left	23	Lobar sclerosis and hemi-atrophy	898	290	240	93	+	...
11	Right	18	Cerebral angioma	1140	565	?	?	+	Sturge-Weber syndrome
12	Left	34	Pseudoporencephaly	862	?	442	109	+	Birth injury
13	Right	28	"	1100	311	375	148	—	"
14	"	34	Lobar sclerosis and état marbré	1005	577	420	140	—	"
15	"	39	Lobar sclerosis	1015	445	400	150	—	"
16	Left	42	Lobar sclerosis and hemi-atrophy	1205	465	465	115	—	"
17	"	23	Lobar sclerosis and microcephaly	704	625	377	115	—	"

\* Formalin hardened: membranes removed.

TABLE VI  
*Infantile Hemiplegia: Acquired. Brain Weights*

	Side of Paralysis.	Age at Onset.	Duration (years).	Morbidity Anatomy.	Total Brain wt. in gm.	Right cerebral hemisphere.	Left Cerebral Hemisphere.	Cerebellum and Brain Stem.	Crossed Atrophy of Cerebellum.	Remarks.
1	Left	Infancy	23	Meningo-vascular syphilis	983	?	?	?	+	Congenital syphilis
2	Right	3 years	17	Hemiatrophy and lobar sclerosis	1140	?	?	?	—	"
3	"	Infancy	20	Hemiatrophy	?	?	?	?	—	"
4	"	3 years	32	Thrombosis sup long. sinus	910	387	387	136	—	"
5	Left	1½ years	37	Int. hydrocephalus	840	325	395	120	—	Fall
6	"	2½ years	15	Tuberous sclerosis	1088	475	470	143	—	...
7	Right	1 year	36	"	1210	535	530	145	—	...
8	"	6 weeks	41	Lobar sclerosis and hemi-atrophy	822	460	225	137	+	...
9	"	1 year	43	Meningitis and int. hydrocephalus	926	534	270	122	+	Meningitis
10	"	2½ years	41	Lobar sclerosis and hemi-atrophy	1068	430	495	143	+	Encephalitis
11	"	2 years	22	Lobar sclerosis	912	422	355	135	—	Whooping cough
12	Left	6 weeks	41	"	940	375	420	145	—	...
13	"	8 weeks	42	Sclerosis white matter	1310	580	580	150	—	Pneumonia and ? encephalitis
14	"	3 years	39	Lobar sclerosis	849	315	402	132	+	...
15	Right	Infancy	26	Unilateral hypoplasia	744	409	295	140	+	...
16	"	10 months	29	"	1044	530	345	169	+	...
17	"	Infancy	20	"	795	415	243	135	+	...

Stated briefly, my material comprised 34 brains, 17 from congenital and 17 from acquired hemiplegia. The most frequent type of cerebral

lesion belonged to one or other of two classes: atrophic sclerosis, either circumscribed or diffuse, and gross defects of the nature of cystic cavities or porencephaly. There can be little doubt that both these types of lesion can originate in a number of different ways. Yet even when naked eye examination is supplemented by the microscope it is seldom possible to determine the nature of the original process. Sometimes, however, the distribution of the lesion affords a clue. For example, when one finds a paraventricular softening in the central white matter, it is safe to infer a lesion of the terminal vein, such as Schwartz (1930) has shown to occur in birth injury. Meningeal hæmorrhage sustained during foetal life or at birth may, if it is large enough, leave some degree of cortical scarring and sometimes microscopic proof of its former presence in the shape of blood pigment lying in the trabeculæ of the pia arachnoid. Such were the findings in one of my patients with hemiplegia who survived a birth injury for thirty-four years.

Occasionally, too, it may be possible to decide whether the sclerosis occurred before or after birth. If, for example, the brain retains its primitive convolution pattern, and if, in addition, there are anomalies of development such as microgyria, we can be fairly certain of an origin in foetal life. On the other hand, if the pattern of the primary, secondary and tertiary convolutions is undisturbed, it is safe to assume that the sclerosis was sustained either at birth or in prenatal life. In lobar sclerosis the individual convolutions are small, shrunken, angular, separated by widened sulci and duly firm to the touch. (Figs. 2, 3). Their appearance has been aptly compared to that of the kernel of a walnut. While in porencephaly it is a softening and liquefaction of the entire brain substance that leads to the formation of the cyst, in lobar atrophy the initial lesion is a loosening of the cortical and medullary tissue with a more or less complete destruction of the nerve fibres and ganglion cells, followed by proliferation of the glia, sclerosis and shrinking (Schwartz). One or two convolutions only may be affected, or to a greater or less extent the whole of one cerebral hemisphere may be involved. With the total involvement of one hemisphere other widespread changes in the nervous system are always associated. On the affected side the basal ganglia, corpora quadrigemina, crus cerebri, pons and medulla all share in the reduction in size and there is often a crossed atrophy of the cerebellum on the opposite side. The condition of the cortico-spinal motor path varies according to the period of foetal or postnatal life in which the lesion occurs. Diseased conditions occurring before maturation of the pyramidal tract entail its non-development, while those of a later date are associated with varying degrees of arrest of development and secondary degeneration. In rare instances on the normal side one sees an enlargement or overgrowth of the normal pyramidal tract. In my experience it is exceptional to find sclerosis extending to the spinal cord. Much more often one sees merely a marked asymmetry or narrowing of the lateral column

of one half of the cord. In those cases in which all the lobes of one hemisphere are sclerosed we have the interesting condition termed hemiatrophy of the brain (Fig. 4). Alpers and Dear (1939) in a recent survey covering a period of more than eighty years found 23 instances of hemiatrophy, but I believe the condition is not nearly so rare as their figures would appear to indicate, for included in my relatively small series were 7 typical examples. In addition, there were three brains with appearances which do not appear to fall into any of the recognised groups. Presenting a condition of marked inequality in the size of the two cerebral hemispheres they differed from the appearances in ordinary hemiatrophy, for in each the smallness of one cerebral hemisphere seemed to be the only abnormality present. There was no thickening of the meninges, no disturbance of the convolitional pattern, no atrophy of convolutions, no widening of the fissures, and no, or only a slight degree of dilatation of the ventricular system. In other words, all evidence of lobar sclerosis was completely lacking. The whole appearance seemed to suggest a condition not of hemiatrophy but rather of an arrest of development or hypoplasia of one cerebral hemisphere.

It is of course obvious that a brain macroscopically normal may on histological examination show many indications of disease, and it is to be regretted that in only one of these three cases has an adequate histological examination been made.

W., the third child in a family of ten, was born after a full term pregnancy and normal delivery. At the age of ten months she had a series of convulsions and became paralysed on the right side. At the age of seventeen she was noted to be an imbecile with a right-sided spastic hemiplegia. The right half of the face was smaller than the left and the right upper limb, with contractures at elbow and wrist, was three-quarters of an inch shorter than its fellow. The lower limbs were of an equal length. The abdominal reflexes were brisk, the right plantar reflex extensor, and the tendon reflexes exaggerated. There were no involuntary movements. She died in her 29th year. In the case in question the brain showed a marked degree of asymmetry, the left cerebral hemisphere being smaller in all dimensions and 185 gm. lighter than the right. The convolitional pattern on the two sides was very similar, but all gyri of the left hemisphere were smaller than on the other side. Apart from this they had a perfectly normal appearance. The asymmetry extended to the mid-brain and pons, but there was little difference between the two halves of the medulla. The cerebellum was normal. Microscopic examination failed to show any abnormality other than diminished depth of the cortical laminæ. On the affected side there was no reduction in the size of the nerve cells, no gliosis and no vascular change. The medulla showed no degeneration of the pyramids, both being of almost equal size.

What is the cause of this unusual finding in which the only abnormality seems to be the marked degree of asymmetry, one cerebral hemisphere being merely the smaller mirror image of the other? It seems obvious, I think, that at some stage of development something had occurred which inhibited the growth of one half of the brain.



To ascribe this to an encephalitis exercising its effects on one hemisphere only and of a character so benign as to leave no trace of its presence would be mere speculation, nor in the absence of pathological evidence of ischæmic changes in the cortex does it seem possible to explain the hypoplasia on the basis of a transitory anæmia, such as Spielmeyer (1928) has postulated to account for the temporary hemiplegias of adult life. One may perhaps hazard the suggestion that the cause of this hypoplasia can best be sought on the lines of some developmental disturbance in the embryonic period of life.

Closely related to atrophic sclerosis is the condition termed porencephaly. It is customary to distinguish two forms, the true and the false. True porencephaly is characterised by the presence of a funnel-shaped opening on the surface of the brain which communicates with the lateral ventricle. The convolutions surrounding it are disposed in a radial fashion (Fig. 5). False or secondary porencephaly shows no such definite arrangement of convolutions, has a cyst-like formation and seldom communicates with the lateral ventricle. Porencephaly is essentially a secondary result and its mode of production is not fully understood, but it appears likely that when not of developmental origin it is a sequel of destructive vascular processes. Not infrequently its position corresponds with peculiar sharpness to the territory nourished by branches of the middle cerebral artery (Fig. 6).

But perhaps the chief interest of porencephaly lies in the striking lack of correlation between the size of the cavity and the degree of functional disturbance. In the motor cortex the loss of brain substance may be impressively large and the paralysis yet be so slight as to cause the patient little inconvenience. Shirres (1902) has recorded an excellent example of this sort of anomalous feature and an equally good illustration occurred in my series.

C. P., aged 13, a male imbecile with a mental age of 5 years, was admitted to hospital in 1923. He was found to possess a fair knowledge of time and place and could write a letter of simple phrases. Physical examination showed a congenital left-sided hemiplegia of moderate degree, the face being unaffected. The left shoulder girdle was less developed than the right and the left upper limb smaller in all dimensions, the difference in length amounting to two inches. The left upper arm was adducted, the forearm pronated and almost fully extended, the wrist slightly flexed, the fingers hyperextended at the proximal joints and slightly flexed at the distal joints. The thumb was adducted and slightly flexed. Though the left hand was weak and the finer and more delicate movements hardly performed at all, the limb was quite useful for carrying or grasping purposes. Thus, when washing utensils, he held them against his body with the left forearm and hand, using the right hand for rubbing. He could hold a broom effectively with both hands and he had no difficulty in dressing. The left leg was inclined to drag a little, but the patient walked and climbed upstairs without difficulty. After death the brain showed the presence of a very large cavity in the right cerebral hemisphere (Fig. 15,) roughly comma shaped, and in which were absorbed the posterior third of the middle frontal gyrus, the lower three-fourths of the

pre- and post-central gyri and the posterior two-thirds of the superior and middle temporal gyri. The cavity was in direct communication with the body of the lateral ventricle with the convolutions surrounding it arranged in the radial fashion which distinguishes true porencephaly of developmental origin. The right middle cerebral artery, after giving off its antero-lateral basal branches, narrowed rapidly to a mere thread and its ascending frontal, ascending parietal and temporal branches could not be found. From the situation of the porencephaly it was obvious that the cortical arm centre was completely absent and yet the patient was able to use his left arm with a freedom truly remarkable.

Before concluding, I should like to refer briefly to the pathogenesis of the hemiplegia which is acquired in early life without any apparent cause. The clinical picture, which has no parallel in the hemiplegia of adult life, is generally initiated by the sudden onset in a child, hitherto healthy, of convulsions, fever, often vomiting and almost invariably coma. After a few days the general condition improves, and it is then noticed that the child is paralysed on one side. Usually by the end of the second week the paralysis reaches its maximum intensity. In exceptionally favourable cases complete recovery may occur with great rapidity, so that at the end of a few days no trace of the paralysis remains. Another peculiar feature is the immunity from second attacks. There has been much discussion about the etiology of this condition, and it may be recalled that as far back as 1884, in an address before the German Society of Naturalists and Physicians, Strumpell (1884) claimed that its pathological basis is a primary acute polioencephalitis. He drew a clinical analogy between polioencephalitis and anterior poliomyelitis and suggested that the two diseases are the result of a single pathological process which at one time has its incidence upon the cerebral cortex, at another upon the grey matter of the spinal cord. In support of his contention, he cited the family reported by Möbius (1884), in which two children were affected at one and the same time, one with a typical anterior poliomyelitis, the other with a spastic cerebral palsy. Were this occurrence an isolated example it might be dismissed as a coincidence, but in the last half-century at least six similar instances have been recorded. Other evidence of a clinical nature has been urged in support of Strumpell's view, but it will perhaps be sufficient to state here that the crucial link in the chain of evidence has yet to be provided: for up to the present in not a single case of infantile hemiplegia have the histological features of anterior poliomyelitis ever been found. In the few recorded instances of children who have died in the acute phase of the illness, most of the brains have shown, not inflammatory, but gross vascular lesions, sometimes hæmorrhage and sometimes softening. Some 16 examples of this kind have been collected by Ford and Schaffer (1927). Usually it is the territory of the middle cerebral artery which is involved, but in one case, briefly reported by Wyllie (1934), thrombosis had occurred in the anterior cerebral artery.

Failure to discover any cause for the hæmorrhage or softening has been a puzzling feature of nearly all the reported cases. Only in one or two instances have the vessels been found to be abnormal. Ford and Schaffer (1927) report the case of a young boy who developed convulsions, coma, and paralysis. Post-mortem examination showed the presence of a large softening in the right fronto-parietal region which had been caused by a thrombus in the right middle cerebral artery. All the arteries of the brain, and to a lesser extent those of the viscera, showed intimal plaques composed of connective tissue and containing a good deal of fat, while in the media there were numerous areas of necrosis with disintegration of the elastic lamina. In the earlier papers of Talbot (1919) and Ghetti (1910) very similar appearances were described. Ford and Schaffer suggest that possibly the arterial degeneration may have been determined by a previous illness, for their patient had acquired scarlet fever a year before his terminal hemiplegia, and as we know, this is one of the infections in which vascular changes of the same order may be encountered. History of antecedent illness of this kind is by no means invariable. To a second and quite distinct group belong brains which show the presence not of massive hæmorrhages but of small cortical softenings, sharply confined to certain laminæ, usually the second and third. Levin (1936) reports the case of an infant who had convulsions at the age of four months and hemiplegia at nine months. Multiple laminar softenings were present throughout the entire cerebral cortex, being especially marked in the parietal regions. The pial arteries showed calcification of the media and proliferation of the intima. Levin interprets these changes on the basis of an ischæmic necrosis conditioned by vasomotor disturbance such as vessel spasm, and he believes that they represent an early and not uncommon stage in the development of atrophic lobar sclerosis. It will be observed that in this type of case both halves of the brain participate in the disease, but not the less interesting are those in which the whole of one cerebral hemisphere is affected and the other entirely normal. To this category belongs the case recently recorded by Le Gros Clark and D. S. Russell (1940). The attack was ushered in by vomiting, convulsions, unconsciousness and high fever, and on the second day of her illness the child became paralysed on the right side. Death occurred five years later. The brain showed a condition of hemiatrophy of the left cerebral hemisphere with crossed atrophy of the cerebellum. Thickened leptomeninges covered the atrophic gyri, and with the exception of a few areas the entire cortex was replaced by spongy glial tissue. In the affected convolutions almost all neurones had disappeared. Atrophy and retraction of the tissues had determined a gross dilation of the lateral ventricle.

Histological examination was not able to throw light on the etiological agent, but in a personal communication Prof. Russell informed me that the mechanism of destruction must have had a vascular basis, and that the histological appearances were indis-



FIG. 3.—Congenital Hemiplegia. Atrophic sclerosis of frontal lobes. "Walnut kernel" appearance. Duration 57 years.

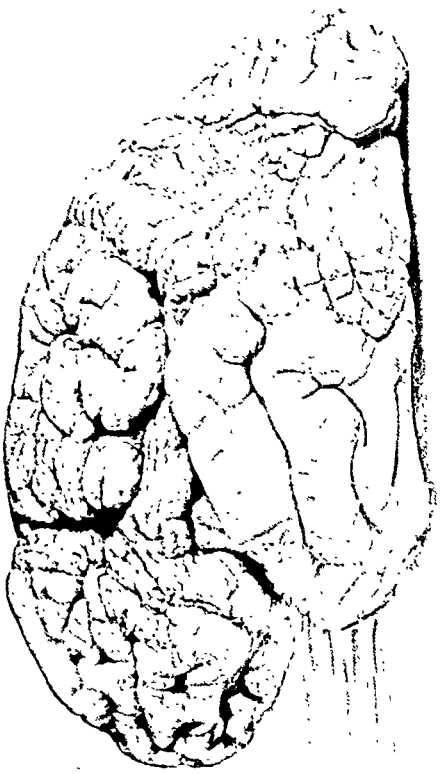


FIG. 5.—True Porencephaly. Duration 18 years.

FIG. 2 and 2a.—Congenital Hemiplegia. Microcephaly, microgyria lobar sclerosis.





FIG. 6.—Pseudoporencephaly in territory of middle cerebral artery. Hemiplegia at third month.

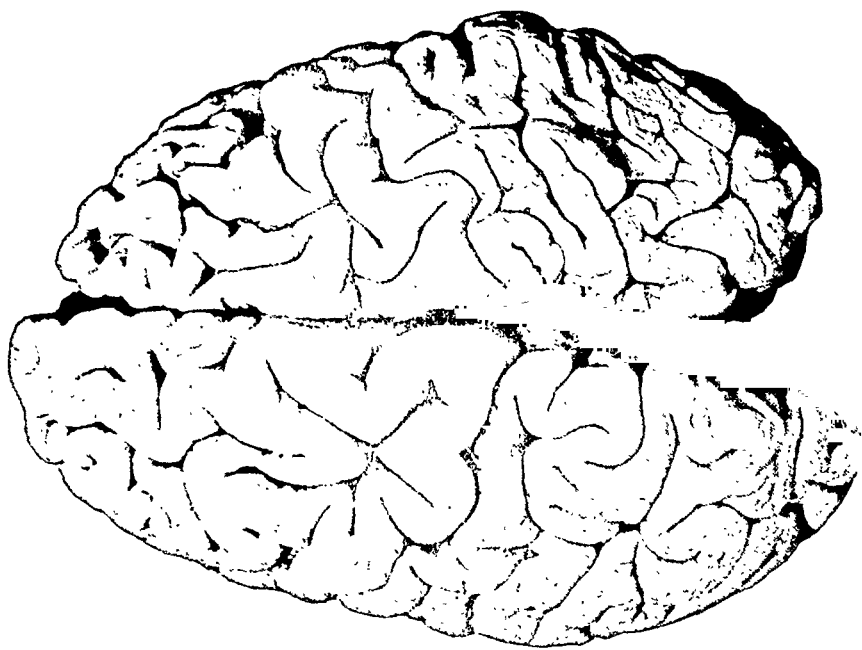


FIG. 4.—Congenital Hemiplegia. Hemiatrophy and Atrophic Sclerosis. Duration 68 years.



tinguishable from those in which anoxia can be fairly claimed to the casual mechanism. Other examples closely resembling this case have been reported by Bielschowsky (1917) and Alpers and Dear (1939).

In summary: from what has been said it would appear that final conclusions cannot be reached concerning the cause of the hemiplegias that are seen in children previously in good health. It is evident that no uniform type of lesion is to be found and that for the encephalitic theory anatomical evidence is almost entirely lacking. In the few reports on autopsies performed on recent cases hæmorrhages and softening predominate, but only in a minority are organic changes in the vessels discovered. Whether lesions of so extensive and grave a character can be caused by functional disturbances of the circulation, such as have been postulated to occur by De Vries (1931) and Bouman (1931), is a question which must be left for future research to decide.

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## NEW BOOKS

*Skin Manifestations of Internal Disorders.* By KURT WIENER, M.D. Pp. 690, with 386 illustrations and 6 colour plates. London: Henry Kimpton. 1947. Price 63s.

The author is not altogether satisfied with the phrase which forms the title of the book and so has coined the word *Dermadromes*—literally, fellow traveller on the skin and this word is used throughout to designate the eruptions which are part of or accompany internal disorders.

A wealth of material is found here as is evidenced by the titles of the chapters which include systemic infections, helminthic diseases, tuberculosis, drug eruptions, diseases of the blood and circulation, of endocrine glands, digestive system, and nervous system. The amount of work involved in the compilation of the book is also shown by the bibliography where there are more than 3000 references.

The book is rather uneven in quality. Too frequently clumsy phrases such as "erythema exudativum multiforme-like" occur. Why not write "like erythema exudativum multiforme"? Details concerning the course of scarlet and other eruptive fevers could be omitted with advantage. The family doctor is usually conversant with them.

No mention is made of Besnier's Prurigo, a not uncommon skin manifestation of an internal disorder. This omission may be because it is an allergic condition, conditions which the author deliberately omits. It would be better to omit the course of eruptive fevers and include conditions like Besnier's Prurigo without condemning the practitioner to wade through books on allergy to get the facts he desires.

The reviewer is surprised at only 13 per cent. of all cases of skin tuberculosis being caused by the bovine bacillus; in Britain the percentage is four times as great, while here, in the reviewer's experience, lupus patients rarely develop phthisis.

The book is well produced and there are many black and white illustrations, but the colour plates are poor.

*Health Services in England.* By R. C. WOFINDEN, M.D., B.S., D.P.H., D.P.A. Pp. x+191. Bristol: John Wright & Sons Ltd. 1947. Price 10s.

This admirably compact and up-to-date review of almost all the health services—preventive and curative, statutory and voluntary—of England and Wales, was awarded the Joseph Rogers Prize in 1946 by the Society of Apothecaries. The author has found space to deal with the treatment of the sick, to mention existing environmental and personal services for the preservation of health, to indicate the scope of economic and social legislation in this respect, to appraise the achievement of the health services of this country and to discuss future trends. Excellent references are provided in the form of footnotes.

*Kompendium der Parasitischen Wurmer im Menschen.* By Dr HANS A. KREIS. Pp. 136, with 70 illustrations. Basel: Benno Schwabe and Co. 1947. Sw. Fcs. 10.

In this small book the author has filled a gap in *German* medical literature which does not exist in British medical literature. He gives a short survey of the life story of the different parasites, and also describes the principles of treatment and prophylaxis of parasitic diseases.

The book is richly illustrated and, taking into account the fact that it is a synopsis, the author has succeeded in telescoping the most important and relevant data in the short space available.

*The Art of Healing.* By BERNARD ASCHNER, M.D. Pp. 336. London: Research Books Ltd. 1947. Price 12s. 6d. net.

After observing folk-lore remedies and delving into medical history, Dr Aschner has attempted to combine the best of these with modern scientific and experimental medicine into what he has called Constitutional Therapy. This book is written for the laity, so the medical reader misses the practical details that would be so helpful. However, one does feel stimulated to try and follow these ideas. Some of the reasonings may not be generally acceptable, but he does get results, and especially in those conditions which are frequently so unresponsive to orthodox treatment. He believes in treating the patient by whatever means will help.

*Radium Dosage. The Manchester System.* Compiled from Articles by RALSTON PATERSON, M.B., F.R.C.S., F.F.R.; F. W. SPIERS, PH.D.; S. K. STEPHENSON, B.SC.TECH.; H. M. PARKER, M.SC., F.INST.P.; M. C. TOD, F.R.C.S., F.F.R.; W. J. MEREDITH, M.SC., F.INST.P. Edited by W. J. MEREDITH, M.SC., F.INST.P. Pp. vii+124. Edinburgh: E. & S. Livingstone Ltd. 1947. Price 15s. net.

The book brings together the original papers describing what has come to be known as the Paterson Parker System of Dosage. There are two sections and in the first, which is of particular interest to radiotherapists, an account is given of the rules for distributing radium containers so as to deliver the required dose uniformly over a given area or volume. The second section provides the physical and mathematical theory underlying these rules. There is no doubt that this book will serve a very useful purpose by providing in convenient form information which has revolutionised treatment by radium.

*Die Bluteiweisskörper des Menschen.* By F. WUHRMANN and CH. WUNDERLY. Pp. 354, with 151 illustrations. Basel: Benno Schwabe and Co. 1947. Sw. Fcs. 36.

This book is the result of the successful teamwork of the University Clinic of Zurich with the co-operation of the Universities of Genf and Bern and of the "Sandoz" Laboratory in Basel, and is a perfect example of the collaboration of the clinician and the biochemist.

Apart from the description given of the chemistry of the plasmaproteins, all the different methods of investigations are described in full detail. In particular, the advantages and disadvantages of the complicated method of electrophoresis are dealt with in an easily understandable way.

The experience obtained by the authors with the newly developed cadmium quick reaction is described from the practical clinical point of view. This method is recommended also as a useful aid in diagnosis for the practitioner.

The thoroughness with which the authors have handled the most difficult problem of the plasmaproteins is praiseworthy.

*The World of Learning,* 1947. Introduction by GILBERT MURRAY, O.M. Pp. x+520. London: Europa Publications. 1947. Price 60s. net.

This book has been compiled to supply comprehensive information about cultural organisations throughout the world. It is divided into sections each of which contains data about conditions in 53 different countries. It lists learned and scientific societies, libraries and archives, museums, universities, etc., giving many details about them and including lists of personnel.

The editors admit that the information may not be as complete and up-to-date as they would wish, but despite the numerous difficulties the compilation of such a work must have encountered, the result is extremely creditable, and the book should prove invaluable as a source of reference.

*Dermatology for Nurses.* By G. H. PERCIVAL, M.D., PH.D., F.R.C.P.E., D.P.H., and ELIZABETH TODDIE, S.R.N. Pp. vii+116, with 90 illustrations. Edinburgh: E. & S. Livingstone Ltd. 1947. Price 15s. 6d. net.

Diseases of the skin are of common occurrence and the onus of treatment rests at present largely on the sufferers themselves. The aim of this small book is to provide instruction for both the nursing and treatment of common skin diseases and thus enable the visiting nurse to lessen the burden of her patient's symptoms. The book is divided into three portions: an introduction on the anatomy and physiology of the skin, a section on treatment of skin diseases in general and lastly, some common diseases of the skin are discussed fully yet concisely. The textbook is well illustrated and should prove of value to all members of the nursing profession.

*The Parathyroid Glands and Skeleton in Renal Disease.* By J. R. GILMOUR. Pp. xiii+157, with 26 illustrations. London: Geoffrey Cumberlege, Oxford University Press. 1947. Price 18s.

The correlation of the renal diseases with the skeletal changes, blood calcium and phosphorous levels and parathyroid alterations is very successfully accomplished in this monograph. Only those renal diseases in which such changes are found are investigated; the classification of Russell is employed and no description is given other than the name of the renal lesion. Parathyroid hyperplasia is expressed as increase in parenchyma weight rather than total weight, this based on the earlier work of the author on normal parathyroid structure. Of six varieties of parathyroid histology two are definitely attributed to renal disease. Hyperphosphatæmia is regarded as the primary abnormality which, associated with hypocalcæmia, leads to parathyroid hyperplasia and changes in the bones of the nature of osteitis fibrosa.

*Anatomical Pattern as the Essential Basis of Sensory Discrimination.* By W. E. LE GROS CLARK, F.R.C.S., F.R.S. Pp. 16. Oxford: Blackwell Scientific Publications. 1947. Price 1s. net.

Professor Le Gros Clark has given an account of the most recent advances in the knowledge of a very fascinating subject. On a basis of histological structure and anatomical relationship of fibres it is possible to explain much that was obscure in the sensory systems.

*Handbook for Nursery Nurses.* By A. B. MEERING, S.R.N. Pp. xi+509, with 118 illustrations. London: Baillière, Tindall and Cox. 1947. Price 17s. 6d.

This book has been planned to cover the syllabus for the certificate of the Nursery Examination Board and should meet the requirements of the student nurse. It deals with anatomy, physiology, nutrition, infection, and hygiene, as well as with certain medical conditions and nursing in the home. A particularly valuable section is that on growth and the management of children. The book is well illustrated and is interesting to read and should be of the greatest value to those for whom it is intended.

*Devils, Drugs and Doctors.* By H. W. HAGGARD, M.D. Pp. xv+405, illustrated. London: William Heinemann Ltd. 1947. Price 12s. 6d. net.

This new edition in cheaper form should appeal to a wide public, especially at a time when medical matters are so much to the fore. Dr Haggard writes interestingly on many subjects in seventeen chapters. He deals with the discovery and development of anaesthesia, and the progress of surgery, the advance of midwifery, the control of infections, and with medicine throughout the ages. Though much of the matter is familiar to the medical man, the story of progress is attractively presented and would be well worthy of the attention of the busy practitioner.

## NEW EDITIONS

*Occupational Diseases of the Skin.* By L. SCHWARTZ, M.D., L. TULIPAN, M.D., and S. M. PECK, B.S., M.D. Second Edition. Pp. 964, with 146 illustrations and one coloured plate. London: Henry Kimpton. 1947. Price 63s.

It is eight years since the first edition appeared and many new industrial processes have been introduced during these years of intense activity. The expansion of industry is reflected in the increased size of the book. There are now 114 occupations listed instead of the 72 in the earlier edition.

Some chapters have been re-written and enlarged while others are new. More details are given of the patch test but it is unnecessary to describe this in two places, while much of the chapter on cosmetics is inapplicable as it refers to the users and not the makers of these substances.

Carelessness is too often apparent in a work of this type. Paraffin sometimes has a final "e" but frequently has not, comedo occurs often as also does comedone. Too much repetition occurs throughout the book. Tetryl, for example, and its hazards are discussed twice in the chapter on explosives and again in the chapter on the analysis of skin hazards in occupation. This applies to other substances as well as tetryl.

In the light of present-day knowledge it is surprising to find Hydroa Aestivale and Pellagra classed as occupational dermatoses. Considerable pruning would greatly enhance the value of the book.

*Short Textbook of Surgery.* By C. F. W. ILLINGWORTH. Fourth Edition. Pp. viii+680, with 12 plates and 227 text-figures. London: J. & A. Churchill Ltd. 1947. Price 30s. net.

The advances in surgical practice that have taken place since 1942, when the previous edition of this excellent textbook was published, are reflected in this latest edition. Penicillin, thiouracil, anticoagulants and protein hydrolysates are now considered; other sections have been re-written and some unsatisfactory illustrations replaced. The volume is slightly slimmer, due to thinner paper and to judicious pruning which has reduced the number of pages by twelve. The paper is of rather poorer quality and less opaque than previously used. This is the only criticism of the present edition of a first-rate students' textbook—authoritative, sufficiently complete, and well-written and produced.

*A Textbook of Pathology.* By WILLIAM BOYD, M.D., DPL. PSYCHL., M.R.C.P. (EDIN.), F.R.C.P. (LOND.), LL.D. (SASK.), M.D. (OSLO), F.R.S.C. Fifth Edition. Pp. 1049, with 500 illustrations and 30 coloured plates. London: Henry Kimpton. 1947. Price 48s.

The fifth edition of this very popular textbook has been brought up to date by the correlation of recent advances in pathology with their clinical applications. The author has dealt at length with new subjects such as lipotropic factors in relation to liver disease, liver lesions in pellagra, renal anoxia including Treuta's observations, and though somewhat more briefly yet quite adequately, with Loeffler's pneumonia, temporal arteritis, pyridoxin deficiency anæmia, and other subjects of topical interest.

Additional new material has been added to such subjects as the pituitary-thyroid axis, bone blood flow in Paget's disease, folic acid in macrocytic anæmia, the Rh factor, and apical localisation of pulmonary tuberculosis, to mention only a few.

Throughout the text the high traditions of academic detail presented in a fascinating literary style which has typified previous editions is maintained. Professor Boyd has achieved the ideal of the Scottish Psalter mentioned in the preface to this edition—"That to perfection's sacred height I nearer still may rise."

*Treatment of Some Chronic and "Incurable" Diseases.* By A. T. TODD, O.B.E., M.B., M.R.C.P. Second Edition. Pp. xi+324. Bristol: John Wright & Sons Ltd. 1947. Price 25s.

In this edition after a lapse of ten years Dr Todd has revised and largely re-written his book and added new material on chronic mental illness. He explains his own views on the aetiology and treatment of a large variety of chronic conditions met in general practice. Many of the views expressed are unorthodox, and he believes that nasal and duodenal sepsis with associated hepatic dysfunction are responsible for a host of diseases. These range from "false phthisis" and "false heart disease" to chronic rheumatism and eczema. Case records are given to show the results of treatment by diet, drugs and ethmoid packs, etc. There are chapters on the theory, therapeutics and results of treatment of inoperable cancer by combined radiation and colloidal preparations. Appendices are given showing the details of diets, prescriptions and colloidal injections.

*Textbook of Mental Deficiency (Amentia).* By A. F. TREDGOLD, M.D., F.R.C.P., F.R.S. (ED.). Seventh Edition. Pp. xvi+534, with 47 plates. London: Baillière, Tindall and Cox. 1947. Price 30s. net.

This well-known textbook by an acknowledged authority easily maintains its place. It is well written, has been kept up to date, and can be accepted as an excellent guide and help to students and post-graduates. It is of interest to note that euthanasia, in the case of idiots and imbeciles, is recommended as an economical and humane procedure. The author believes that adequate safeguards could be easily devised but the reviewer has grave doubts regarding both the practicability and advisability of such a serious step.

*Materia Medica, Pharmacy, Pharmacology and Therapeutics.* By WILLIAM HALE-WHITE, K.B.E. Twenty-seventh Edition, revised by A. H. DOUTHWAITE, M.D., F.R.C.P. Pp. x+549. London: J. & A. Churchill Ltd. 1947. Price 15s.

This well-known and popular book has again been completely revised and new material has been included as the result of the rapid advances which have been made in pharmacology and therapeutics. In spite of the additions to certain sections, particularly in those dealing with antibiotics, the size of the book has been kept unaltered by means of careful pruning of less important sections. Particular attention has been paid to the clinical application of drugs, and the paragraphs on therapeutics are for the most part extremely clear and sound. Heparin is usually prescribed in international units rather in milligrammes, and no mention is made of any antidote. These are, however, only minor criticisms of an excellent book.

*Surgical Disorders of the Chest.—Diagnosis and Treatment.* By J. K. DONALDSON, B.S., M.D., F.A.C.S. (Lieut.-Col., A.U.S.). Second Edition. Pp. 485, with 146 illustrations and 2 coloured plates. London: Henry Kimpton. 1947. Price 42s. net.

The second edition of this textbook on the surgical aspects of chest disorders has been brought completely up to date. The subject-matter is well presented and the main points are given prominence throughout by the use of sub-titles. Each section ends with a summary.

A short bibliography of the more recent literature is appended to each chapter. The references are carefully selected and are a valuable addition to the text.

The author corrects the current belief that thoracic surgery is concerned only with the lungs, and gives details of cardio-vascular and gastro-oesophageal surgical technique.

If criticism can be made, it is that too much has been attempted for a work of this size. It would appear that the descriptions of the more common conditions have been curtailed in an effort to cover the widest possible field.

The volume gives a well-balanced outline of a rapidly developing subject.

*Pathological Histology.* By ROBERTSON F. OGILVIE, M.D., F.R.C.P. EDIN., F.R.S.E.  
Third Edition. Pp. xii+459, with 260 photomicrographs in colour. Edinburgh :  
E. & S. Livingstone Ltd. 1947. Price 37s. 6d. net.

Dr Ogilvie's textbook of *Pathological Histology* needs no introduction. Since the first edition appeared in 1940 undergraduate and graduate alike have found this textbook of great value in the study of morbid histology.

The text of the present edition has been extensively revised and fifteen new plates have been included in the alimentary, hæmopoietic, nervous and endocrine systems to keep the textbook abreast of recent advances in pathology.

*Aids to Gynæcology.* By W. R. WINTERTON, M.A., M.B., B.CH., F.R.C.S., M.R.C.O.G.  
Tenth Edition. Pp. v+184, with 17 illustrations. London : Baillière, Tindall & Cox. 1947. Price 5s. net.

In spite of the number of moderately sized textbooks of gynæcology now available there is evidently still a demand for *Aids to Gynæcology* as the appearance of a tenth edition indicates. It has been revised and provides in a condensed and abridged form the essentials of modern gynæcology. The harassed student with little time for revision will find it helpful.

*Practical Histology for Medical Students.* By D. T. HARRIS, M.D., D.SC., F.INST.P.  
Fourth Edition. Pp. vi+138, with 2 plates. London : H. K. Lewis & Co. Ltd.  
1947. Price 12s. 6d. net.

This book is intended primarily as a practical class drawing book and is provided with blank interleaved pages for that purpose. The printed text opposite indicates method of preparation and principal features of the slides listed, but is not meant to replace a systematic textbook. For teachers who prefer a formal printed class programme the book includes all the histological specimens likely to be of interest to medical students.

*The Principles of Anatomy. An Introduction to Human Biology.* By A. A. ABBIE, M.D., B.S., D.SC. (SYD.), PH.D. (LOND.). Second Edition. Pp. x+273, illustrated.  
London : Angus & Robertson Ltd. 1946. Price 12s. 6d.

This book, first published in 1940, was designed to illustrate biological principles from the study of human anatomy. As such it was soon recognised as a useful adjunct to the textbooks of the student of medicine ; and its success is indicated by the appearance of a second edition largely re-written and with extended scope.

More attention is now paid to such topics as genetics and growth gradients and the influence they exert on human development ; and there are new summaries of times of ossification, eruption of teeth, etc., which are useful for reference. Appendices contain an etymological glossary and a brief history of anatomy ; some of the chapters have short lists of key-references ; and there is a good index. The illustrations are mostly schematic but well-adapted for their purpose.

*Synopsis of Neuropsychiatry.* By LOWELL S. SELLING, M.D., PH.D., D.P.H., F.A.C.P.  
Second Edition. Pp. 561, with 27 illustrations. London : Henry Kimpton.  
1947. Price 32s. 6d. net.

In the second edition of this book the changes affecting neurology consist mainly in bringing the sections on treatment up to date in the light of recent advances. A new chapter is added on disorders of speech and reading. The section on mental disorders has been enlarged with new chapters on psychosomatic medicine and psychiatric treatment. In the various chapters of this book the facts are presented in precise and tabulated form which is an aid to rapid reference to any particular subject. It does not profess to give more than the basic facts on any disease and within these limitations succeeds in presenting the subject in a form which should prove useful to students and to doctors.

*Diseases of the Nervous System.* By W. RUSSELL BRAIN, D.M., F.R.C.P. Third Edition. Pp. 987, with 79 illustrations. London: Oxford University Press. 1947. Price 37s. 6d. net.

This textbook has earned an important place for itself among all those who recognise in modern neurology, not so much a special subject as a closely integrated system of medicine. Such a theory requires no amplification since the proof is available for all those who care to scrutinise the pages of this comprehensive work.

Nothing is assumed in the reader who is given a composite picture of each branch with due emphasis on the basic sciences, and with a clearly defined clinical description of each entity. In these days there must be few authors who have either the experience or the energy to provide a book of this scope, with its attention to detail and completeness, but Dr Brain's numerous readers recognise in him the embodiment of wide knowledge and style of presentation. We are sincere in wishing this textbook the success it deserves.

## BOOKS RECEIVED

- BASTEDO, WALTER ARTHUR, PH.G., PH.M., (HON.)M.D., SC.D., (HON.)F.A.C.P.  
Pharmacology Therapeutics and Prescription Writing. Fifth Edition.  
(*W. B. Saunders Company, London*) 42s.
- BECKMAN, HARRY, M.D. Treatment in General Practice. Sixth Edition.  
(*W. B. Saunders Company, London*) 57s. 6d.
- CADY, LOUISE LINCOLN, R.N. Nursing in Tuberculosis.  
(*W. B. Saunders Company, London*) 20s.
- CAMPBELL, JAMES TODD, PH.B., M.D., and SANFORD, ARTHUR HAWLEY,  
A.M., M.D. Clinical Diagnosis by Laboratory Methods: A Working  
Manual of Clinical Pathology. Eleventh Edition.  
(*W. B. Saunders Company, London*) 37s. 6d.
- CLAYE, ANDREW M., M.D., F.R.C.S., F.R.C.O.G. Management in Obstetrics.  
(*Geoffrey Cumberlege, Oxford University Press, London*) 12s. 6d. net.
- DOWLING, HARRY F., M.D., F.A.C.P. The Acute Bacterial Diseases: Their  
Diagnosis and Treatment . . . (*W. B. Saunders Company, London*) 32s. 6d.
- FISHER, A. G. TIMBRELL, M.C., M.B., CH.B., F.R.C.S.(ENG.). Treatment by  
Manipulation: In General and Consulting Practice. Fifth Edition.  
(*H. K. Lewis & Co. Ltd., London*) 25s. net.
- GOODALE, RAYMOND H., B.S., M.D. Nursing Pathology.  
(*W. B. Saunders Company, London*) 15s.
- LOVE, R. J. McNEILL, M.S.(LOND.), F.R.C.S.(ENG.). Minor Surgery. Third  
Edition . . . (*H. K. Lewis & Co. Ltd., London*) 22s. 6d. net.
- MUIR, ERNEST, C.M.G., C.I.E., M.D., F.R.C.S. EDIN. Manual of Leprosy.  
(*E. & S. Livingstone Ltd., Edinburgh*) 17s. 6d. net.
- RYLE, JOHN A., M.D. Changing Disciplines.  
(*Geoffrey Cumberlege, Oxford University Press, London*) 12s. 6d. net.
- SANDS, IRVING J., M.D. Neuropsychiatry for Nurses. Fifth Edition Illustrated.  
(*W. B. Saunders Company, London*) 15s.
- SCHERF, DAVID, M.D., F.A.C.P., and BOYD, LINN J., M.D., F.A.C.P. Clinical  
Electrocardiography. Third Edition.  
(*William Heinemann Medical Books Ltd., London*) 30s. net.
- STONES, HUBERT H., M.D., M.D.S., F.D.S.R.C.S. ENG. Oral and Dental Diseases.  
(*E. & S. Livingstone Ltd., Edinburgh*) 90s. net.
- SWANSON, MARGARET J. MCKENZIE, B.LITT., F.C.H.S. Textbook of Chiropody.  
(*E. & S. Livingstone Ltd., Edinburgh*) 20s. net.
- THIENES, CLINTON H., M.D., PH.D., and HALEY, THOMAS J., PH.D. Clinical  
Toxicology. Second Edition . . . (*Henry Kimpton, London*) 22s. 6d. net.
- TRAIL, RICHARD R., M.C., M.A., M.D.(ABERD.), F.R.C.P.(LOND.). Chest Examination:  
The Correlation of Physical and X-ray Findings in Diseases of  
the Lung . . . . . (*J. & A. Churchill Ltd., London*) 12s. 6d.

# Edinburgh Medical Journal

September 1948

## THE EARLY HISTORY OF THE MUSEUM OF THE ROYAL COLLEGE OF SURGEONS OF EDINBURGH

By J. N. J. HARTLEY, *O.B.E.*, *F.R.C.S.*

TOWARDS the end of the fourteenth century, Edinburgh was confined to the immediate vicinity of the ridge running east from the Castle. The Burgh was only about one mile long and half a mile in breadth. Narrow closes and wynds extended from the High Street down each slope to the King's Wall, which served as a protection against the frequent assaults of the "Common Enemy." The houses were piled to enormous heights, some having twelve stories, with dark, steep and dangerous common stairs. Here, the early Barber-Surgeons carried out their primitive surgery—dressing wounds, arresting bleeding, drawing blood, adjusting fractures and extracting teeth.

### SEAL OF CAUSE OF BARBER-SURGEONS

Various Crafts had been recognised as civic incorporations, such as Skinners, Masons and Wrights, Candlemakers, Tailors, Cordiners, and the great Society of Hammermen who wrought in metal, Goldsmiths, Blacksmiths, Pewterers, Lorimers, Cutlers and Armourers. The Crafts were closely linked with the Church: the chief official of each Craft was called Deacon or Kirkmaster and the members were bound to support a chaplain and altar in the Kirk of St Giles. The Crafts had certain privileges and were protected, no one being allowed to enter a Craft without having served an apprenticeship. In 1505 the Barber-Surgeons, anxious to secure these privileges, made a joint application to be "incorporated." The Town Council granted the request and the Seal of Cause was confirmed the following year by James IV. The Barber-Surgeons were now allowed to dissect each year one condemned prisoner "after he be deid" for the purpose of instructing their apprentices in anatomy. Though legal permission to dissect the human body had been granted at an earlier date in certain foreign schools, the Edinburgh Incorporation of Barber-Surgeons had the distinction of being the first to acquire this privilege in Britain. A curious clause in the Charter gave the Barber-Surgeons the exclusive right to make and sell "*aqua vitæ*." Thus was formed the Society which eventually became the Royal College of Surgeons of Edinburgh.



It is interesting to note that the site of future great activity of the Surgeons was already well-defined in the open country to the south-east of the Burgh. The Cowgate at that time was a narrow green valley. On its southern slope was the Monastery of the Black Friars which had flourished for nearly three centuries. The Priory and large Guest House were near the lane leading down the valley. The rising ground to the south of the Priory was walled off into four portions, known as the Friars' Yards. On the eastern Yard, the Barber-Surgeons, nearly two centuries later, built their first Hall, and in another half-century the Old Royal Infirmary was built on the western Yard. Immediately to the west of the Friars' Yards was the Kirk o' Field, and here the Town Council, in 1583, opened their College which later was replaced by the present University, the foundation stone being laid in 1789.

The Barber-Surgeons did not begin to record their Proceedings until 1581, but did so continuously thereafter. The early records are far from easy to read as is evident from the first entry, the College Prayer, ascribed to John Knox, and still read by the Secretary at the opening of each Statutory Meeting of the College :—

“ O Eternal God, and our loving and merciful Father in Christ Jesus, seeing we are convenit heir to treat upon these things that concernis our calling, we beseik thee, O Lord, to be mercifull to us, and giff us grace to proceed thereintill without malice, grudge, or partialitie ; sua that the things we may do may tend to the glorie of God, the weill of our vocation, and comfort of every member of the samen ; throw Jesus Christ our only Lord and Saviour.—AMEN.”

#### GILBERT PRYMROSS' MORTAR

When the Proceedings began to be recorded the Barber-Surgeons had already taken first place among the Crafts. It is generally accepted that their advancement was due to the activities of Gilbert Prymross (Gilbert Primrose), Chirurgeon to James VI, and three times Deacon of the Incorporation. Prymross was a member of a Perthshire family, the present representative of which is the Earl of Rosebery. In the Museum of the College there is an interesting copy of Gilbert Prymross' brass mortar found on the Borders and believed to have been lost by Deacon Prymross while in action against the invaders.

Though the Barber-Surgeons had begun well, they contributed little or nothing to the advances made in anatomy and surgery during the next two centuries. There was no pioneer in Edinburgh to share the fame of Vesalius, Fallopius, Spigelius, Vidius, Paré and others who flourished on the Continent during the sixteenth century, or of Harvey, Cooper, Warton, Willis, De Graaf, Malpighi, Stensen and Wirsung in the seventeenth century. It must, however, be remembered that the Craft in Edinburgh was small and served only the Burgh, and the people were miserably poor and were constantly distracted by war and internal strife.

Towards the end of the seventeenth century, two centuries after the granting of the Seal of Cause, conditions in Scotland became more propitious. The association of the Surgeons with the Barbers had not been happy and, in 1695, this was dropped, and the Surgeons were then called Chirurgeons and Chirurgeon-apothecaries. By Royal Grant the Incorporation extended its power from the City to the three Lothians, and to the Counties of Perth, Selkirk, Roxburgh, Berwick and Fife, and more young men were seeking an entry to the Craft. The Physicians at this time for the most part had had to obtain their education abroad, and after repeated application had, in 1681, formed the Royal College of Physicians of Edinburgh. One of the most distinguished of the Physicians at the end of the seventeenth century was Archibald Pitcairne. After obtaining the M.D. of Rheims in 1680, he returned to Edinburgh and became a member of the College of Physicians and also had the distinction of being elected a member of the Incorporation of Surgeons. His eminence, due to contributions to literature, procured for him, in 1692, an invitation to assume the Chair of Physic in the celebrated University of Leyden. The language difficulties in those days were solved by Latin being the common medium for both writing and lecturing. In his class at Leyden were Boerhaave, who later was to wield such an influence over the Edinburgh School, and John Monro, father of Alexander Monro, *Primus*.

#### OLD SURGEONS' HALL, 1697

Pitcairne returned to Scotland with the idea that if more material were available in Edinburgh an Anatomical School could be developed comparable to that of Leyden. He instigated Alexander Monteith, Deacon of the Incorporation, to approach the Town Council with a view to obtaining more bodies for dissection. This request was granted and almost immediately thereafter, in 1694, the Incorporation itself made a similar application which was also granted, but with a condition "that the petitioners shall before the term of Michaelmas 1697 build, repair and have in readiness an anatomical theatre, where they shall once a year (a subject offering) have ane public anatomical dissection as much as can be shown upon one body." To comply with this condition the Incorporation built their first Hall on the site of the East Friars' Yard, in 1697. There is no definite evidence that Monteith availed himself of the privilege of teaching anatomy. Subsequently he commenced a course of chemistry in the basement of the College Hall.

#### EARLY COLLECTION OF RARITIES AND CURIOSITIES

After the erection of the Hall, provision was made for housing such books as the College possessed as well as certain rarities which formed the nucleus of a museum. Two years later it was decided to record all donations and in a long list are found:—"A large African Gourd, with a silver head; a case containing ten old German lancets;

a large eel skin stuff and taken in Cramond Water ; a pair of Scots cocks spurs clecked in Fife, prodigiously long ; several shells, plants of *Spongie marina* got in the North of Scotland ; an American Wasps' nest ; an Allegatory, or young Crocodile." An advertisement was ordered to be put in the *Edinburgh Gazette*, asking for "natural and artificial curiosities." Donors if they thought not fit to bestow them gratis were to be paid reasonable prices for them.

### SYSTEMATIC TEACHING OF ANATOMY

In 1708 the Surgeons entrusted the entire duties of dissection and instruction to one of their members, Robert Eliot. He made application to the Town Council for pecuniary help and was granted £15 yearly, but with the express provision and condition that the petitioner take exact notice and inspection of the order and condition of the rarities of the College, and that an exact inventory be made of the same and given in to the Council.

During the ensuing fifteen years the appointment was held conjointly by Robert Eliot and Adam Drummond, and by Adam Drummond and John McGill. These two resigned in 1720 in favour of Alexander Monro, *Primus*, whose father, John Monro, was a distinguished army surgeon of King William's Army, and a former Deacon of the Incorporation, and had long cherished the desire that a School of Physic and Surgery should be instituted in Edinburgh. With this object in view he had trained his son Alexander so as to fit him for a Chair of Anatomy.

### TRANSCERENCE OF THE SCHOOL OF ANATOMY TO THE UNIVERSITY

Alexander Monro in 1720, on the recommendation of the Surgeons, was appointed Professor of Anatomy by the Town Council. He carried out his duties as Professor of Anatomy in the Surgeons' Hall until 1725. In that year the City was in an uproar in consequence of the supposed violation of graves and the mobs threatened to demolish Monro's establishment in Surgeons' Hall. To secure better protection, therefore, he moved to the University. At the College Monro had been joined by four physicians, who like himself had studied in Leyden under Boerhaave: Drs St Clair, Rutherford, Innes, and Plummer. These now petitioned the Town Council to be made Professors in the University and their request was granted. Thus the Faculty of Medicine in the University was formed by the transference of the School which Monro had gathered round him in the Old Surgeons' Hall.

Sir Alexander Grant, a former Principal of the University, says of Monro *Primus*, that "he was not only the Father of the Edinburgh Medical School, but also the first professor of any kind who drew great attention to the University of Edinburgh from without, and gave it the beginnings of its celebrity."

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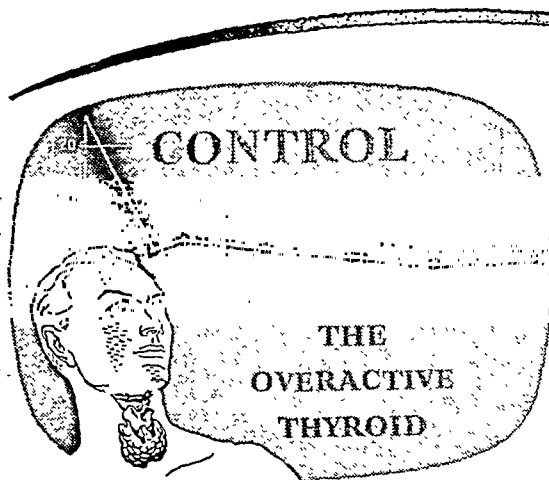
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## SEPARATION OF BARBERS: ROYAL CHARTER

While the University rapidly gained renown because of its Medical School, the College of Surgeons passed through a period of adversity which lasted several decades. Two important events, however, occurred. In 1722, after much litigation, the Barbers were completely separated from the Surgeons. The Society of Barbers gradually faded away, and when it eventually ceased to exist, the box which had been presented to them for safe preservation of their documents was returned to the College as "*ultimus haeres*" and is now one of the historical exhibits in the Museum. The other event of note was the charter which, in 1778, raised the Incorporation to the rank of a Royal College.

## SKELETONS GIFTED BY PITCAIRNE AND MONRO, PRIMUS

The College now became so impoverished that the greater part of the Hall was let as private residences. At times, even the Hall had to be rented and it was therefore decided in 1763 to hand over to the Keepers of the University Library the collection of books and curiosities belonging to the Incorporation. Two preparations were, however, retained, and they are now the oldest existing in the College Museum. The one is a skeleton of a young subject with mummified muscles still attached mounted in a case and gifted by Archibald Pitcairne in 1702. The other is a skeleton, also of a young subject, mounted in a similar case and gifted to the "*Incorporation of Chyrurgien Apothecaries*" by Alexander Monro in 1718. Thus ended the first primitive museum of the Barber-Surgeons. Though varieties and curiosities were undoubtedly again collected, no mention of a museum is made in the records until 1804.

## RISE OF THE EXTRA-MURAL SCHOOL

Monro, *Primus*, was followed by his still more distinguished son Alexander Monro, *Secundus*. By their teaching and contributions to literature the School of Anatomy attracted increasing numbers of students.

In 1798 Monro, *Secundus*, was succeeded by his son Alexander Monro, *Tertius*, but unlike his father and grandfather he was an uninspiring teacher. Due largely to this, new and important anatomical schools sprang up around the Old Surgeons' Hall. In 1790 John Bell erected a house to the south-east of Surgeons' Hall and for nine years this brilliant surgeon taught, for the first time in Edinburgh, Surgical Anatomy. He was succeeded in 1779 by his younger brother, Charles Bell, who later was to become still more renowned. In 1778 the Royal Medical Society built their Hall on the west side of the area to the north of the Surgeons' Hall, and in the house erected by Dr Andrew Duncan between the Royal Medical Society and the Surgeons' Hall, Dr John Barclay, in 1800, established his School of Anatomy and there he accumulated anatomical preparations that later were to form an

important part of the College Museum. During the latter part of the eighteenth and the early part of the nineteenth century Surgeons' Square became associated with great names, especially in Anatomy, Physiology and Surgery, which contributed much to the reputation of Edinburgh as a Medical School.

### TEACHING OF SYSTEMATIC SURGERY IN THE COLLEGE

Despite the dread of sepsis and the lack of control of pain, surgery in the eighteenth century had made great advances and famous schools had arisen in London and on the Continent. In 1748 the Old Infirmary with its 228 beds had been erected on the western Friars' Yard and the clinical facilities it afforded were a great stimulus to the younger Surgeons in Edinburgh. Neither *Monro, Secundus*, nor *Monro, Tertius*, was a practising surgeon, yet they claimed the prerogative of teaching surgery along with anatomy. The need of a separate Chair of Surgery in Edinburgh grew more and more urgent. Representation was made by the College to the Town Council on several occasions, but in vain. It is true that a Chair of Clinical Surgery was founded by the University in 1803. James Russell, one of the Surgeons of the Royal Infirmary, was the first occupant of the Chair and this he held until 1833 when he retired at the age of seventy-eight. During the period when the College was actively concerned in establishing a teaching museum, Russell was the Convener of the Curators. The Professor of Clinical Surgery, however, was not allowed to interfere with the rights of the Professor of Anatomy and Surgery and was prohibited from giving a course on Systematic Surgery.

Having failed to induce the University to separate surgery from anatomy, the Surgeons decided, in 1804, to establish the post of Professor of Surgery in the College, and appointed John Thomson as their first Professor. During the next twenty-seven years, surgery as a separate subject was taught only in the College. It was not until 1831 that the University created their Chair of Surgery, and Thomson's successor in the College, John William Turner, was the first to occupy the Chair. The Royal College of Surgeons has reason to be proud of having instituted the teaching of both anatomy and surgery in Edinburgh, especially when one considers the renown of the Edinburgh School and of the many distinguished anatomists and surgeons who have subsequently held the University Chairs.

John Thomson had studied in Glasgow and Edinburgh, and then for a period of one year in London, where he worked in the School of John Hunter and no doubt there acquired interest in pathology and in the collecting of specimens. On returning to Edinburgh, he joined the College and was appointed one of the Surgeons to the Royal Infirmary. Two years after being appointed Professor of Surgery in the College he became first occupant of the Chair of Military Surgery in the University and continued to serve in both capacities until he

resigned the College appointment in 1821. In 1831 he was again to be the first occupant of a Chair, that of Pathology in the University. Having been the first holder of no less than three professorships he was known as the "Old Chairmaker."

### ORIGIN OF TEACHING MUSEUM

In the College records, 1804 is referred to as the year in which the present Museum had its origin. There is a long entry of the meeting of the College on 3rd October 1804 in which rules are laid down for the newly elected Professor of Surgery. Amongst these are :—  
 "That it would greatly facilitate the teaching of Surgery and prove useful as well as creditable to the College to form a Museum of Morbid preparations, casts, and drawings of diseases ; and that all the members of the College should be requested to give their assistance in promoting this very necessary part of the plan by supporting it with all such articles of this kind as may be in their power." "That this Museum shall be the property of the College and be open under such regulations as the College may adopt, to the inspection of all its members."  
 "That five members shall be elected annually who along with the President and Professor of Surgery shall form a Committee for the management of the Museum, and who shall see that every thing be duly taken care of ; but the trouble of preparing all morbid specimens of chirurgical diseases presented to the College and of keeping them in proper arrangement shall devolve exclusively upon the Professor."

In the Museum Catalogue which was begun about this time and which still exists, it is unfortunate that the early entries are not dated. Some of the specimens entered may have been presented earlier than 1804. It is quite certain that many specimens collected by Thomson and others were accumulated and used for teaching and presented many years later to the College for general use.

In 1807 nine members of the College were appointed Curators of the Museum. In 1814 a Committee was set up to revise the Museum Laws and it was decided to add the Professor of Clinical Surgery, provided he was a member of the College.

### APPOINTMENT OF KEEPER

In 1816 a Keeper was appointed and the first to occupy the post was John William Turner, an assistant to Professor John Thomson in his Class of Surgery. This post Turner held until 1821 when he succeeded his master as Professor of Surgery to the College.

In 1817 it was reported in the Minutes that "the Museum contained upwards of 300 preparations of diseased organs and textures many of them very interesting and instructive and in general in a good state of preservation." It was stated that a catalogue of the preparations according to their number had been made out and deposited in the Museum.



## ANXIETY ABOUT THE INADEQUACY OF THE TEACHING MUSEUM

Despite the appointment of a Professor of Surgery and a Keeper, the Museum was increasing very slowly. The Extra-Mural School had rapidly developed and was playing an important part in the teaching of anatomy and surgery. The Surgeons were fully aware of the inadequacy of the Museum, especially when compared to the large museums which existed in England and on the Continent. William Hunter's famous Pathological Museum had been bequeathed to the Glasgow School, and the unrivalled Museum of John Hunter had been acquired by the Government at a cost of £15,000 and presented to the Royal College of Surgeons of England. It was little wonder, therefore, that the College grew anxious and began to look without the city for the means of rendering their Museum worthy of the dignity of their Institution.

In 1821 there began a period of great activity in the College in respect of their Museum and this continued during the whole of the next decade. On 31st January 1821, Professor Russell as Convener of the Curators called for an Extraordinary Meeting of the College to discuss a proposal to purchase a Museum which was offered for sale by Dr Meikel of Halle in Germany. The anatomical collection consisted of 5000 preparations, and from the skill and care which had been bestowed in selecting and preparing the specimens it was considered to be without equal in Europe. The price asked for it was £5000 sterling. The negotiations with Dr Meikel, however, did not succeed.

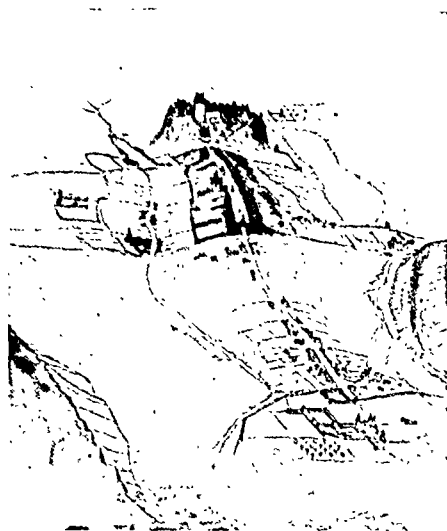
### DR BARCLAY'S OFFER

While this was under consideration a letter was received from Dr John Barclay and read at a meeting held on 10th July 1821. He felt encouraged to offer his Museum and to bequeath it simply on the condition that the College would build a Hall to receive it and that the Collection should be allowed to retain his name.

On 18th July 1821 the Collegé acknowledged receipt of this letter "and returned their best thanks not only for the liberality of his intentions but for the very handsome and unqualified terms in which he had presented to them so valuable a gift."

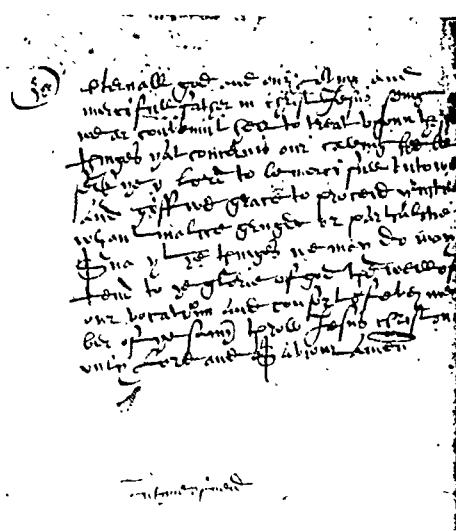
Dr Barclay at this time was the most popular teacher of anatomy in Edinburgh and 300 students were attending his class. Barclay's character was altogether admirable—good natured, generous, almost never angry, good humoured, his wit never offensive, and, unlike most of his contemporaries, he did not indulge in bitter controversy.

He was born in 1759 in humble circumstances and educated at a parish school in Perthshire. When aged seventeen he obtained a foundation bursary and entered the Old College in St Andrews. Here he greatly distinguished himself in Greek. After graduating he was licensed as a Preacher by the Presbytery of Dunkeld and for some

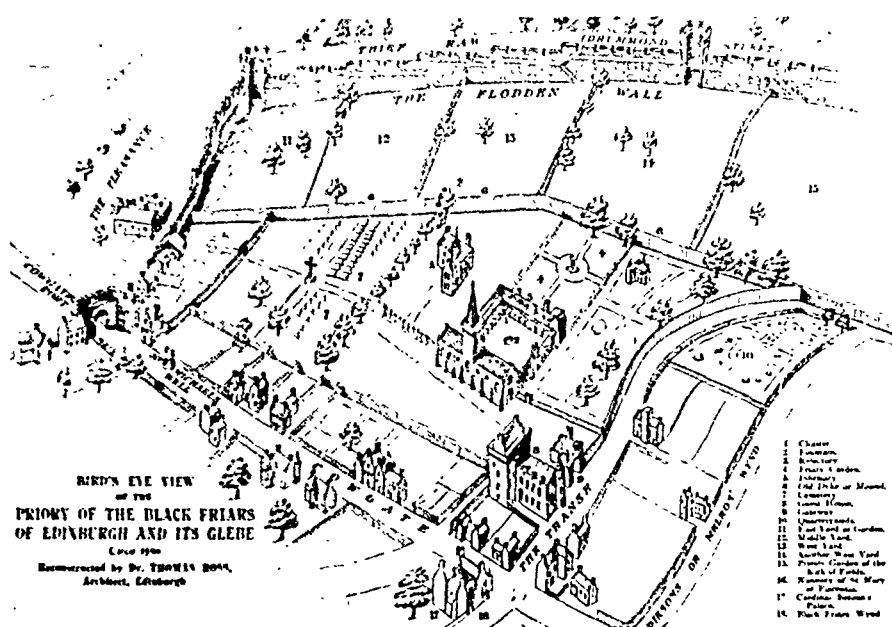


Reconstructed view of Edinburgh. Circa 1450. Note the King's Wall, Cowgate Valley, Black Friars Monastery with the Friars' Yards to the south, and the Kirk o' Field to the south-west

From *Edinburgh 1329-1929*, Commemorative Volume 1929



The First Entry in the College Records—The College Prayer ascribed to John Knox—1581



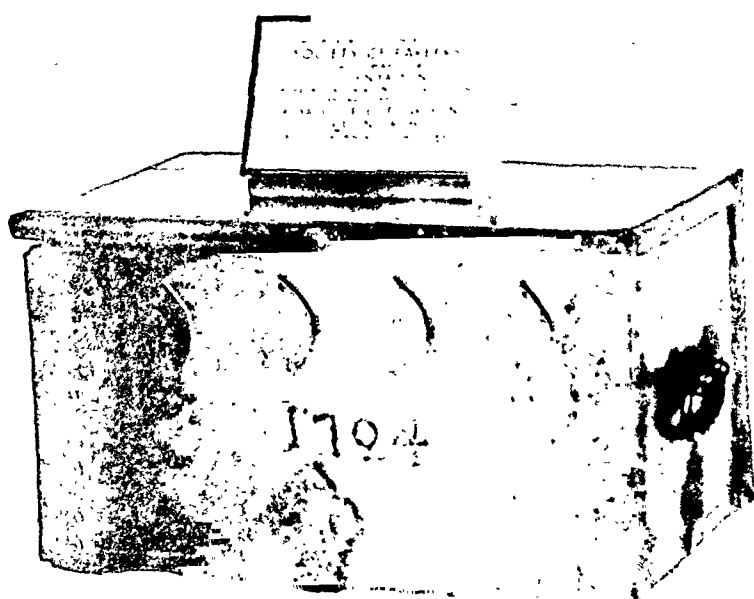
BIRD'S EYE VIEW  
OF THE  
PRIORY OF THE BLACK FRIARS  
OF EDINBURGH AND ITS GLENS  
Circa 1540  
Reconstructed by Dr. THOMAS BOW,  
Architect, Edinburgh

Bird's Eye View of the Priory of the Black Friars—Circa 1540. On the East Friars Yard was built the first Surgeons' Hall, and on the two Western Yards the Old Royal Infirmary. Part of the Flodden Wall still exists

By courtesy of the Old Edinburgh Club



The Lintel and Tympanum of the Old Surgeons' Hall  
Museum of the Royal College of Surgeons, Edinburgh



Treasure Chest of the Barbers, after their Separation from the Incorporation of Surgeons  
Museum of the Royal College of Surgeons, Edinburgh



Surgeons' Hall. Erected 1697  
Original picture in the Royal College of Surgeons, Edinburgh



Alexander Monro, *Primus* (1697-1747). "The Father of the Edinburgh Medical School."  
From a painting by Allan Ramsay

*The Story of the University of Edinburgh* by Sir A. Grant



Archibald Pitcairne (1652-1713). After returning from the Chair of Physic in Leyden stimulated the study and teaching of Anatomy in Edinburgh

From *History of Scottish Medicine* by John D. Comrie



John William Turner (1790-1836). The first Keeper of the College Museum. In 1831 he became the first Professor of Surgery in the University

Original portrait in the Department of Surgery,  
University of Edinburgh



John Thomson (1765-1846). The first Professor of Surgery (1804-21), in the College of Surgeons. Known as "The Old Chair Maker" because he was the first holder of three professorships

Original in the Royal College of Surgeons, Edinburgh



Sir Charles Bell (1774-1842), whose Collection of pathological and anatomical preparations assembled in the old Hunterian Anatomical School in Windmill Street was acquired by the College in 1825 and still forms a part of the present Museum

Copy from *The Letters of Sir Charles Bell*,  
John Murray, London, 1870



Professor William Macgillivray (1796-1852).  
The second Conservator of the Museum  
From *Vertebrate Fauna of the Outer Hebrides* by  
J. A. Harvie-Brown and T. E. Buckley. 1888

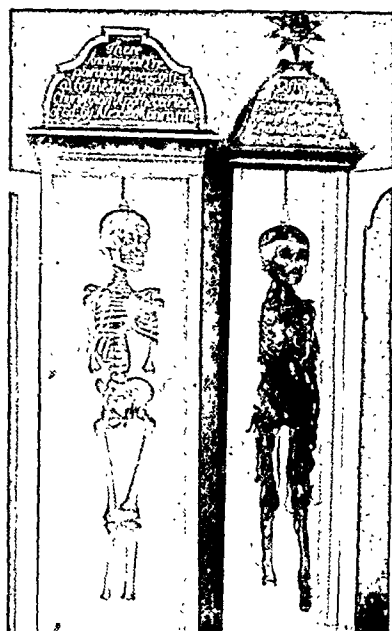


South-west Corner of Surgeons' Square, 1829. From left to right—the Old Hall, Gordon's Class Room, Barclay's School of Anatomy, and the Hall of the Royal Medical Society

From *Old and New Edinburgh*. Messrs Cassel, Petter and Galpin

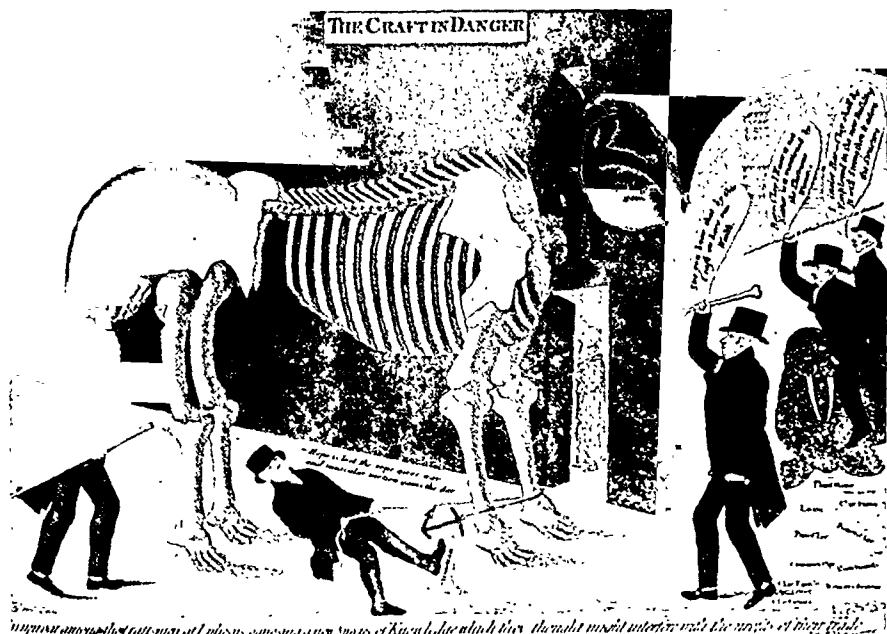


Broggan's Skull—one of the relics of the Burke and Hare episode  
Museum of the Royal College of Surgeons, Edinburgh



Skeletons gifted by Archibald Pitcairne, 1702, and by Alexander Monro, *Primus*, 1718

Museum of the Royal College of Surgeons, Edinburgh



"The Craft in Danger." Kay's Caricature of Dr Barclay storming the University with a view to establishing a Chair of Comparative Anatomy

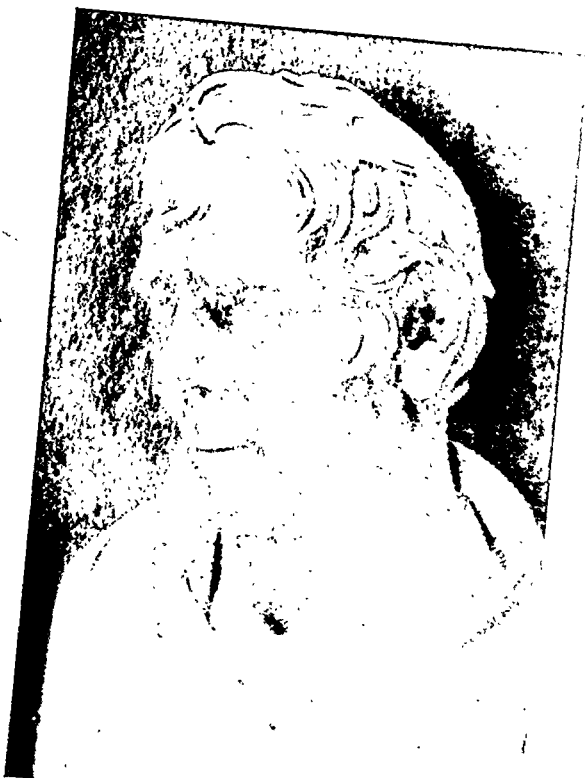
From Kay's *Original Portraits*, vol. ii. A. & C. Black, Edinburgh. 1877



Wax Model of a patient with Hernia Cerebri  
made by Sir Charles Bell  
Museum of the Royal College of Surgeons, Edinburgh



Bust of Burke. From a cast made the day  
after he was hanged  
Museum of the Royal College of Surgeons, Edinburgh



Dr John Barclay (1759-1826)  
From a bust by Joseph in the Museum of the Royal  
College of Surgeons, Edinburgh



Dr Robert Knox (1791-1862). The first  
Conservator of the Museum of the Royal  
College of Surgeons, Edinburgh

time was employed as a tutor. When aged thirty he moved with his employer, Sir James Campbell, to Edinburgh. He had always been interested in natural history and soon after coming to Edinburgh began to give his attention to anatomy—both human and comparative. Anatomy soon absorbed his attention and for a time he was assistant to John and Charles Bell. In 1796, at the age of thirty-seven, he graduated at the University of Edinburgh and thereafter studied anatomy for a period under Dr Marshall, a distinguished London anatomist. One year later, at the age of thirty-eight, he began his lectures on anatomy in a small class-room in the High School Yards. Though he had formidable competition he was not daunted and in 1800 acquired the lecture theatre between the Surgeons' Hall and the Hall of the Royal Medical Society, and here he continued to lecture until 1825.

Among his many distinguished assistants and pupils were James Syme, Robert Liston, Richard Owen, who became the Conservator of the John Hunter Museum at the Royal College of Surgeons of England, Robert Christison, George Ballingall, Mr Nasmyth, the father of Scottish dentistry, and Dr Robert Knox. Barclay was a member of the Highland Society, and largely due to his urging the study of veterinary medicine, the Veterinary School of Edinburgh was established and ably conducted by William Dick, also one of his pupils.

John Barclay was probably the first in this country to give a systematic course on comparative anatomy. One of his exhibits was a skeleton of an elephant presented by George Ballingall, and the elephant still exists in the Royal College of Surgeons' Museum. Barclay's friends tried to persuade the Town Council to make him a Professor of Comparative Anatomy, but this was vehemently opposed by Hope, Jameson and Monro. The famous John Kay made a clever caricature showing Barclay astride his elephant forcing his way through the College gates. Two of his obstructors were Jameson, who cried "Bar-clay," and Hope whose restraining rope breaks :—

" Hope is lost, the rope gives way,  
And Muscular Motion gains the day."

The Chair, however, was never created.

Many stories were told of Barclay. One illustrated his well-known liberality to young men struggling with adverse fortune. " Mr Laing, an eminent book-seller and friend of Barclay, sent him a needy student with a request for a ticket of admission to his advertised lectures. Barclay readily granted the free ticket, but at the same time asked the youth to accompany him to Mr Laing's shop. There he selected anatomy class books to the value of three guineas and said to him : ' You can do no good at my lectures without class books ; these are the same price as my ticket ; Mr Laing makes you a present of them. ' "



Near the end of his career, Barclay's pupils presented him with a Memorial and raised a fund with which they obtained a marble bust executed by Joseph. The bust was eventually handed to the College and is now to be seen in the entrance hall.

### CULLEN'S SCHEME

In 1822, William Cullen, a grand-nephew of the celebrated Cullen, wrote a long communication to James Russell, the Convener of the Curators, suggesting that the best method of rapidly acquiring pathological material for the Museum was to send an emissary to Paris and offered his services. Cullen had studied several years in Paris and had returned to Edinburgh to join the College. He pointed out that in Paris there did not exist as in England strong prejudices against dissection and examination of bodies and that material was abundant, the only difficulty being to collect and turn it into profit for the College. At La Pitie, 2500 bodies were dissected annually and at the School of Medicine, 1200. If regular visits were made to all the Pavilions of Anatomy, in the course of three or four years the College could be enriched with gleanings of nearly 10,000 bodies.

Dr Cullen's offer was accepted and he was provided with £300 a year as salary and £500 a year to be expended in providing preparations and transmitting them to Edinburgh. After becoming a Fellow of the College in the Autumn he proceeded to Paris. The conditions in Paris, however, were found not to be as favourable as Cullen had imagined. In a letter written on 23rd October 1822 he expressed fear that the object of his mission was impossible, and that if he failed in some further attempts he intended to solicit his recall, and almost immediately afterwards a letter was received stating that Cullen had suffered a stroke of apoplexy which was attributed to the apprehension of his failure. The scheme, like that in connection with Dr Meikel's Museum, ended in failure.

During the next year little of interest is to be found in the College records. Some preparations were received; two rooms at the west end of the Hall were thrown into one and fitted with glass cases and shelving in preparation for Barclay's Collection; and in June of 1823 Mr Watson was appointed Joint-keeper to Robert Hamilton who, two years previously, had succeeded John William Turner.

### ADVENT OF DR ROBERT KNOX

In April 1824 a most unusual and dramatic figure appeared on the scene, Dr Robert Knox, who was to play a dominant part in the Museum affairs during the next seven years. He was born in 1791, and while at the High School in Edinburgh was head of every class and became Gold Medallist. In 1810 he entered the Medical School of the University of Edinburgh. In *Monro Tertius's* class he failed in anatomy. After a course in Barclay's School he re-sat his University

examination and it is recorded that his examiners were amazed by his profound knowledge of anatomy set forth in the choicest Latin. After graduating, in 1814, he obtained a Commission as Assistant Surgeon in the Army and was immediately sent to Brussels to render aid to the wounded at Waterloo. Thereafter he was transferred to the Cape of Good Hope where he remained for a period of three years. While there he took a wide interest in Natural History and Ethnology. During one year's study leave he visited various centres on the Continent including Cuvier's Museum in Paris, the Hunterian Museum in London, and the Pathological Museum of the Military Hospital at Chatham. After five years of practical experience as a Military Surgeon he returned to Edinburgh in 1822, and managed to subsist on half-pay from the Army and on the earnings of a small practice. Most of his time was spent in doing research, and many papers were contributed to scientific journals and learned societies. Lonsdale in his biography of Knox states that "The Museum of the Royal College of Surgeons, in the 'Old Hall' of the 'Incorporation of Chirurgeons,' was a very poor affair in 1823. Its modern collection, or specimens of health and disease, and a few natural history examples, belonged almost entirely to the nineteenth century and these scarcely numbered 300 in all. This condition of affairs might well shock Knox, fresh from the Parisian School, and he longed above all things to redress it."

On 2nd April 1824 Robert Knox wrote a letter to Mr Russell, Convener of the Curators of the College, in which he said that he was willing to bestow his whole labour and time, with that energy which the cultivation of a very favourite pursuit naturally gives; the attending expenses of presses, glass, spirits, etc., to be borne by the Royal College of Surgeons. He was moreover willing that the Museum so erected should be considered as the property of the College and intended for the use of its Fellows, reserving to himself during his lifetime the use of the Museum for the furtherance of his favourite pursuits and studies. Should this proposal thus briefly sketched meet generally with the approbation of the College he would be extremely happy to meet every view or suggestion which might be offered, and contribute to the utmost of his abilities in advancing the best interests of the College.

Dr Knox's plan was generally approved and a satisfactory agreement was reached. Eight months later he was asked to take charge of the Pathological Museum in co-operation with the Keepers at a salary of £100 a year. In a letter at this time the term Conservator is used, but it was not until an open election on 15th May 1826 that he was appointed first Conservator with a salary of £150 a year. In March 1825 Knox became a partner with his former master, Dr Barclay, and when Barclay died in 1826, Knox came into complete possession of Barclay's School of Anatomy. During the next five years of his intensely busy life, Knox combined the duties of Conservator of the Museum with those of an extremely popular Extra-Mural teacher.

Moreover, he was constantly carrying out research, and making contributions to literature and scientific bodies.

Robert Knox was one of the most striking lecturers that Edinburgh has ever seen. Lonsdale in his fascinating biography gives a vivid picture of this remarkable man :—

“ The apparent restlessness of both his features and framework, bespoke the versatile Frenchman more than the ‘ canny Scot.’ The atrophied condition of the left eye, the large nose and full mouth were heightened in force by strong lines and a coarseness of features incident to the worst form of confluent smallpox. His perfect eye was perfection itself, and an excellent index to his passing thoughts. The muscles of Knox’s face were seldom at rest when his brain was occupied. These involuntary twitchings were far from agreeable, especially those which affected his under-lip, the crossing of which from side to side produced a kind of smacking noise.”

“ Dr Knox was wonderfully got up in the way of costume, and was perhaps the only lecturer who ever appeared before an anatomical class in full dress. Being a well-made person, his tailoring was all the more effective for his display of ‘ The glass of fashion and the mould of form.’ A dark puce or black coat ; a showy vest, often richly embroidered with purple, across which gold chains hung in festoons ; a high cravat, white or in coloured stripes, and the folds of which were passed through a diamond ring ; a prominent shirt collar, delicately-plaited cambrics, watch-seals and pendants, set off by dark trousers and shining boots, completed his outer man. Knox, in the highest style of fashion, with spotless linen, frill, and lace, and jewellery redolent of a duchess’s boudoir, standing in a class-room amid osseous forms, cadavers, and decaying mortalities, was a sight to behold, and one assuredly never to be forgotten.”

“ If Nature had been less kind in her gifts to the outer man, she was lavish in her bestowals upon the social and intellectual Knox. However harsh if not forbidding in personality, his courtesy and conversation atoned for all.”

His fame was such that within four years his class had risen to 504 and this necessitated him repeating his lecture three times daily. Many were attracted to his lecture room and his prelections were regarded as the greatest intellectual treat in the “ Modern Athens.”

Though a born orator, Dr Knox is believed to have prepared himself for special occasions. It is related that :—

“ at a late hour of a winter’s evening, two of Knox’s junior assistants had gone down to the dark cellared mortuary for the purpose of injecting the arteries of a new ‘ subject,’ and, whilst so engaged, were much startled by hearing noises in which vocal sounds faintly mingled with a sort of tramping march. In the full belief that they were the sole occupants of the building, and being quite unable to unravel the unearthly acoustics, and further tried by

‘ The horrible conceit of death and night,  
Together with the terror of the place,’

something akin to Juliet’s dread stole over them. ‘ Hush ! ’ there is another heavy beat, a pause, articulate sounds, now emphatic, now sinking away in a distant cadence, then followed by stillness. The disconcerted medicals in breathless haste left the charnel-house and rushed upstairs. As they approached

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# PRESSURE DRESSING FOR A SCALD

August 22nd, 1947. Scalded at work. Next day attended hospital with a large blister of inner aspect R. ankle. (Fig. 1).

**Treatment.** Scalded area dressed with Jelonet (tulle grás), Viscopaste bandage applied from toes to knee. Pressure pad of cotton-wool applied over scalded area. The whole leg firmly bandaged with Elastocrepe, with especially firm pressure over the scalded area. (Fig. 2).

October 7th, 1947. When bandages were removed, wound soundly healed. (Fig. 3).



Fig. 1

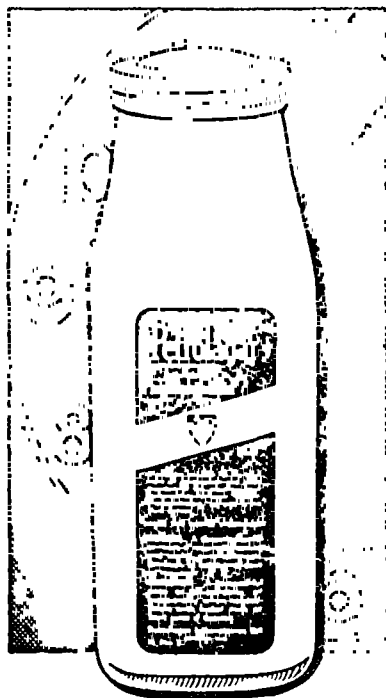


Fig. 2

**Comment.** Firm pressure dressing afforded *immediate* comfort, permitting ambulatory treatment and continuation at work. These details and illustrations are of an actual case. T. J. Smith and Nephew, Ltd., of Hull, manufacturers of Elastoplast, Elastocrepe, Jelonet and Viscopaste, publish this instance—typical of many—in which their products have been used with success.



Fig. 3



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**HABIT TIME**  
*OF BOWEL MOTION*

Habit time of bowel motion may be restored by the use of 'Petrolagar' which, by softening and adding bulk to the bowel contents, promotes evacuation by normal peristalsis.

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the door of the lecture-room they listened, and detected a human voice, and that voice could be no other than the weird anatomist's: the 'questionable shape' was discovered to be a 'spirit of health' and not a 'Goblin damn'd!' Yes! the syrenic Knox was heard busily tuning his instruments for to-morrow's 'Oratorio.' Verily a strange rehearsal, and stranger scene! Standing in the small enclosure of darkness that 'a farthing dip' rendered visible, Knox was going through the part of his own Hamlet, practising the attitudes, now delivering his thoughts in calm and measured tones, now loudly vehement, as the subject of his prelection demanded."

#### ACQUISITION OF THE MUSEUMS OF CHARLES BELL AND JAMES WILSON

After the arrival of Dr Knox the affairs of the Museum moved quickly. In January 1825 Professor Russell announced that Mr Charles Bell's anatomical and pathological preparations had been offered for the sum of £3000. A month later, Dr Knox and Mr Watson were sent to London to inspect the collection. The report was favourable and the offer was accepted. The Museum acquired from Charles Bell consisted of two collections, his own and that of James Wilson.

Charles Bell was born in 1774 and was the son of a Scottish Minister who died young. Charles was the youngest of four very talented brothers. The eldest brother, Robert, became Professor of Conveyancing to the Society of Writers to the Signet. His brother John was the most outstanding Surgeon in Edinburgh at the end of the eighteenth century, and his brother George was Professor of Scots Law in the University of Edinburgh. Charles was trained in anatomy and surgery by his brother John and became a Fellow of the College of Surgeons of Edinburgh in 1799. About this time he took over the anatomical class from his elder brother John, and continued to teach in Surgeons' Square until 1804. During this period he had already made a name for himself by his *System of Dissections* in three volumes, and his *Engravings of the Arteries, of the Nerves, and of the Brain*. He had also almost completed one of his masterpieces, the *Anatomy of Expression*. In 1804 he decided to go to London. New regulations at the Royal Infirmary had excluded his brother John from the hospital staff, and a bitter controversy ensued, the two parties being led by John Bell and Professor James Gregory. There was little prospect of Charles being appointed to the Hospital, and both the Chair of Clinical Surgery and the Chair of Systematic Surgery in the College had recently been filled. These considerations, and perhaps the examples of William and John Hunter, induced him to seek a career in the metropolis. There he was soon on friendly relations with Abernethy, Astley Cooper, Baillie, Wilson and others. For several years he encountered considerable difficulties as revealed in his published letters to his brother George. Charles Bell bought a dilapidated house in Leicester Street and there had resident pupils and conducted classes. During the early period in London he published

All the bodies found their way to Dr Knox's theatre. There can be no doubt that Knox had been quite unaware of having received the bodies of murdered people, but unfortunately the infuriated mobs considered him guilty and everywhere was heard :—

“ Down the Close and up the Stair,  
But and ben wi' Burke and Hare.  
Burke's the butcher, Hare's the thief,  
Knox the man that buys the beef.”

Mobs attacked his house in Newington and broke all the windows, and his effigy was hanged from a lamp-post in front of his house. For some time after the Burke disclosures he was greatly in danger of being molested in the streets. Christison says, however : “ he would have been a formidable adversary to assail ; for, though short, he was strong, agile and resolute, and carried pistols, which he would most assuredly have used with effect in his defence.”

On the 28th January 1829 Burke was hanged in the Lawn Market in the presence of 20,000 to 25,000 spectators. Early next morning the body was taken to the College to be publically dissected by Professor Monro, *Tertius*. Before the students began to assemble, several eminent scientists—among them Mr Liston, Mr George Combe and Sir William Hamilton—inspected the body, and Mr Joseph, the Sculptor, took a cast of the head and neck. A bust of Burke is one of the exhibits in the College Museum. After being exhibited and partly examined, Burke's remains were preserved for future anatomical study. A wallet made from some of his tanned skin and containing a copy of the *Courant* newspaper in which is his confession, was recently presented by Mr G. L. Chiene to the College Museum.

A further interesting relic of the Burke and Hare episode in the Museum is that of a skull with deformity of the lower jaw, the deformity having arisen from contraction of the skin of the lower lip and front of the neck due to a burn in childhood. It is the skull of John Broggan, whose wife was a cousin of Burke. In his confession Burke stated that four of the murders were committed in Broggan's house which Burke and his dissolute partner Helen McDougal occupied for some time. Burke knew that Broggan had suspicions and had bribed him. Though Broggan was arrested he was soon released as he was obviously innocent of the murder. Broggan died in a cholera epidemic and his skull was acquired by the College. Some time later, when the public was admitted to the Museum, the skull was recognised and claimed by Broggan's relatives. They could not resist the temptation, however, to make financial gain, and the skull was sold to a dentist who eventually bequeathed the specimen to the College.

During the succeeding two years the College was chiefly concerned with plans for the new Hall in Nicolson Street on a site which previously had been occupied by a riding school. Knox could have had very little leisure to devote to the Museum. His class at this time was about 500. He was rapidly acquiring an extensive Museum of his

own and he employed a Conservator to whom he gave more than he received from the College. One of his specimens was that of a Great Whale and this, he used to say, cost him nearly £500. He lived frugally and the remaining large profits of his class he devoted to his Museum and the advancement of Science.

In May 1831 Mr Watson moved in committee "That the Curators be requested to pay attention to the Laws regarding the Museum," which motion was seconded by Dr Mackintosh. There was also a discussion on the duties of the Conservator. It was pointed out that the rule relating to attendance of the Conservator for visitors and Fellows had been in abeyance.

Dr Knox no doubt regarded this as censure. It was obviously impossible to carry out efficiently his duties as Conservator as well as all his arduous work in his School of Anatomy and it is not surprising therefore, that he offered his resignation.

#### APPOINTMENT OF WILLIAM MACGILLIVRAY AS CONSERVATOR

Dr Knox's resignation was accepted and steps were immediately taken to secure a successor. On 2nd August 1831 out of nine candidates Mr William MacGillivray was elected Conservator. Though possessing no medical qualification, Mr MacGillivray was in many ways admirably suitable for his new duties. He was born in 1796 in Old Aberdeen. When a boy he was taken to Harris to reside with an uncle, his father having been killed in the Battle of Corunna. After eight years in the Outer Hebrides, William entered Aberdeen University and graduated M.A. For a time he acted as Dissector to the Lecturer of Anatomy at King's College, Aberdeen. With a diary, and a copy of Smith's *Flora Britannica*, he walked from Aberdeen to London in order to see the country and to visit the British Museum. On his way back he broke his journey at Edinburgh and attended lectures given by Robert Jameson, Professor of Natural History and Regius Keeper of the Museum of Edinburgh University. He later served as Assistant and Secretary to Professor Jameson and while holding these posts MacGillivray applied for the Conservatorship of the Museum of the Royal College of Surgeons.

His duties during the first year as Conservator were especially arduous and laborious and tested both his physical and mental powers. The large Museum of the College was scattered in several buildings, and the condition and arrangement of the specimens were far from satisfactory. The new Surgeons' Hall was in the process of erection on the site of the Riding Academy in Nicolson Street. It is recorded in his biography that MacGillivray cleaned all the specimens, re-arranged and labelled 4000 preparations and supervised the transference of the whole Museum to the new Hall prior to the official opening which took place on 7th July 1832.

During his ten years as Conservator, MacGillivray gave loyal



service to the College and this received due recognition. He completed the Catalogue and in 1836 had printed what is now known as the *Former Printed Catalogue*. It included all the specimens, casts and drawings then in the Museum illustrating pathology, but none of those illustrating human and comparative anatomy.

MacGillivray's heart, however, was in Natural History and not in Surgical Pathology. This is evident by the many entries in the Manuscript Catalogue of natural history objects. While serving as Conservator he published three volumes on the *History of British Birds*. By his contribution, it is said, he revolutionised ornithology by insisting on the necessity of taking into account, in the classification of birds, the internal as well as the external organs. In 1841 he resigned his appointment of Conservator on being made Professor of Natural History in Marischal College, Aberdeen.

The year 1841 may be regarded as the end of a definite period in the history of the Museum. Now it was safely housed and fully displayed. The Conservator who had been responsible for its removal and arrangement and for the first printed Catalogue had resigned and was to take up duties in another city. Robert Knox's popularity had waned. From 1832 he continued to hold his class in the Old Hall, but in the year 1841 he moved to Argyle Square and soon thereafter left the city to lead a nomadic life and eventually to die in obscurity. There is no Catalogue of his Museum. In 1867 Sir John Struthers stated that Robert Knox's considerable Collection was in his possession. Later it was dispersed; some preparations are in the University Anatomical Museum; only a few unimportant preparations remain in the College Museum. John William Turner, the first Keeper, who later served as Professor in the College and then as first Professor of Systematic Surgery in the University, died young in 1836. John Thomson, the "Old Chairmaker," was failing in health and in one year was to resign the Chair of Pathology. Professor Russell who had guided the Curators for so long had attained his four score years and died in 1836. Sir Charles Bell's fame had continued to grow after leaving Great Windmill Street School and on John William Turner's death he was invited to take the Chair of Systematic Surgery in the University of Edinburgh. His term of office in Edinburgh was to be short for he died in 1842. He must have been gratified to know that his Museum, on which he had spent so much time and labour, was to be a lasting memorial to him in his native city.

Before quitting the Museum, reference may be made to a particularly interesting relic which it contains. The Old Hall became the property of the University and when it was being reconstructed, Principal Sir William Turner preserved the tympanum and lintel of the old doorway. Dr A. Logan Turner, during his presidency in 1927, gave effect to the expressed wish of his father, by presenting the tympanum and lintel to the College, and these are now to be seen

under the stairs leading to the College Hall. Under this lintel and tympanum passed Monteith on his way to his chemical laboratory, Eliot, McGill and Drummond, the first teachers of systematic anatomy in Edinburgh, John Monro, and his son Monro, *Primus*, the father of the Edinburgh School of Anatomy. Towards the end of the eighteenth century and at the beginning of the nineteenth century there would often pass John Bell, the first to give a course on surgical anatomy in Edinburgh, Charles Bell and John Barclay who were both to make important contributions to the Museum, Professor Russell, quaintly dressed, who was long the Convener of the Curators, and Syme, Liston, Fergusson and many others whose memory will always be held dear by graduates of the Edinburgh School.

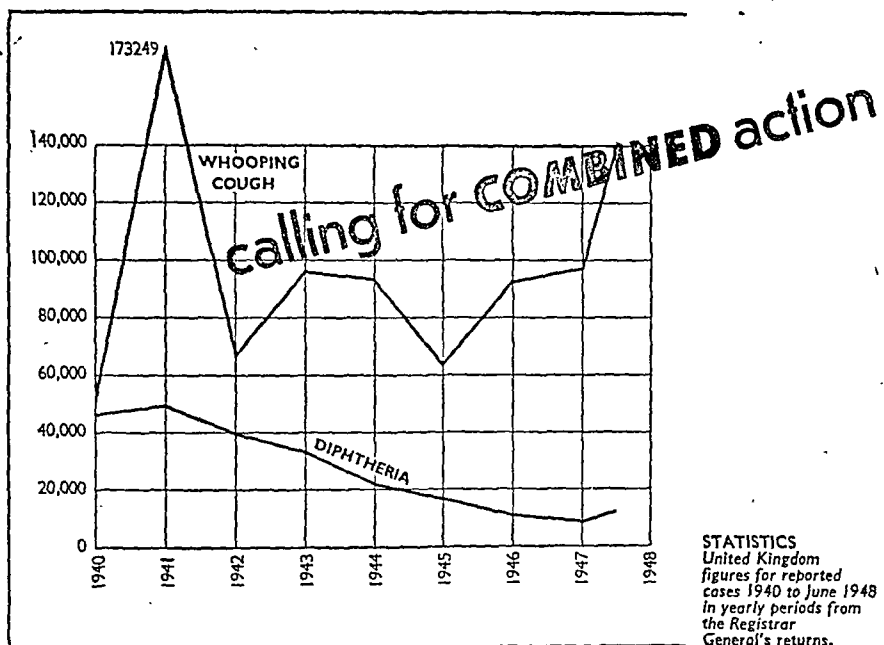
It might be said that the Museum was conceived rather late in the history of the College, when in 1804 John Thomson was appointed the first Professor of Systematic Surgery. There had been previous "miscarriage" in the way of collections of curiosities, one prior to the transfer of the School of Anatomy to the University, and one later in the same century. The gestation of the present Museum was long, stormy and eventful, and came to an end when the Museum appeared in its home in the College New Buildings in Nicolson Street. The offspring proved to be lusty and a credit to its venerable parent. The life of a museum is normally long, and it is good to think that the College Museum, though almost one-and-a-half centuries old, is still in adolescence and that it will continue to mature and to grow in importance as an instrument of education in the Edinburgh School of Surgery.

It is with pleasure that I acknowledge my gratitude to the Assistant Librarian of the Royal College of Surgeons, Miss Frances Brown, for valuable help in searching the College Records, also to the Librarian of the Signet Library, Dr C. D. Malcolm, for much information about Old Edinburgh, and to Mr A. Miles, F.R.C.S.E., for helpful criticism and suggestions.

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# GASTRO-JEJUNAL ULCERATION

By A. G. R. LOWDON, O.B.E., F.R.C.S.E.

## INTRODUCTION

GASTRO-JEJUNAL ulceration is a subject of peculiar interest and importance for several reasons. It is a man-made disease, a failure of the surgical treatment of ulcer. Moreover it is a serious failure, because it is frequently a more troublesome and dangerous condition to the patient than the original complaint. It carries with it the risk of the usual complications of peptic ulcer—hæmorrhage and perforation—and in addition others as serious if not more so. The surgical treatment of gastro-jejunal ulcer, often imperative, is difficult and dangerous. And withal we can extract only one doubtful consolation—that study of this unfortunate development may shed a little light on the problem of the aetiology and treatment of peptic ulcer in general.

## HISTORICAL

In 1884, three years after the first gastro-jejunostomy had been performed for cancer, Rydygier carried the development a step further by successfully performing the same operation for a simple pyloric stenosis due to peptic ulceration, and the era of gastro-enterostomy for peptic ulcer was introduced. Surgeons all over the world were quick to see the possibilities of the measure. Though the mortality of the operation was at first high, they persevered because no satisfactory or even promising alternative was known for the treatment of pyloric stenosis.

The main difficulty in the performance of the operation seemed to be a mechanical one—how best to place and make the stoma to ensure its efficient and continued function. Many alternative methods were proposed and widely tried during the next twenty years: anastomosis to the front and to the back of the stomach; anastomosis to the fundus, to the body and to the antrum; entero-anastomosis between loops and anastomosis “en-Y”; long and short loops of jejunum, lying antecolic and retrocolic; vertical, horizontal and oblique openings; anastomosis with catgut, thread, Murphy's button and even rings of bone. Finally, in the beginning of the twentieth century, the technique became fairly standardised as advocated by Moynihan or the Mayos. A posterior anastomosis, one end of which reaches the most dependent part of the stomach, is made with a short proximal loop of jejunum.

While all this controversy raged about the mechanical difficulties another storm was brewing. In 1899 Braun and Hahn reported cases

A Honyman Gillespie Lecture delivered in the Royal Infirmary, Edinburgh, on 27th February 1947.

of death which autopsy showed to be due to the perforation of an ulcer in the jejunum just beyond a gastro-jejunostomy stoma. About the same time Mikulicz reported the successful closure of the perforation of an ulcer at such an anastomosis. Scattered reports of such complications continued to appear in the literature, including a few in British publications, but it was not till 1909 that the attention of surgeons in this country was focused on the problem. Then H. J. Paterson presented to the Royal Society of Medicine a paper on gastro-jejunal ulcer with a detailed account of two personal cases and a very complete abstract of the 61 cases that had been reported up to that time. "The fear of the possible occurrence of a jejunal ulcer," he wrote, "still casts a shadow—faint it is true—over the otherwise admirable results which follow this operation when performed in appropriate cases."

It is humbling to find how little we can add, twenty-eight years later, to Paterson's conclusions from his masterly analysis of those early cases. Sad to tell, however, he did not even attempt to elaborate his own phrase, "when performed in appropriate cases." Had his vision, already remarkable, crossed one more horizon and led him to advocate that gastro-enterostomy should be avoided in cases with high acidity or without pyloric stenosis, the subsequent history of the disease might have been radically altered.

As it was, the very success of the operation of gastro-jejunostomy proved its undoing. The beneficent results in cases of ulcer with stenosis led to its wider and wider use till it was employed in very many cases of ulcer, duodenal and gastric, without distinct indications. This development was further justified in practice by the dramatic relief that was given to most of these patients. It was only after many years that the increasing incidence of anastomotic ulceration revived a memory of Paterson's warning.

On the continent of Europe growing concern about this complication led to the increasing use of partial gastrectomy in place of simple anastomosis for ulceration. In this country and in America surgeons were more conservative, but growing interest in the subject was reflected in the *Collective Inquiry by the Fellows of the Association of Surgeons* which was compiled and published by Garnett Wright of Manchester in 1935. The practice of partial gastrectomy grew steadily in this country also, and has proved in a large measure a solution of the problem—with qualifications which we must leave for consideration later. But even after partial gastrectomy, anastomotic ulcers have been observed and these too, though relatively rarer, must be considered.

### THE CLINICAL PICTURE

The story and the clinical features of a case of secondary ulceration are fairly typical and all too familiar.

The patient tells us that some months or years ago he had an

operation for ulcer trouble, or for a perforated ulcer, and that a "short circuit" was made. For a time he was happily free from symptoms, then his pain returned. Usually this new pain is more widespread and centred more at the midline or more to the left and lower down than before. It is often more severe and more constant, and comes on earlier after food than the previous pain. Sometimes it is eased by food or alkaline powders, but often this relief is incomplete. Vomiting occurs in about half of the cases and frequently gives temporary comfort, so that it is sometimes self induced. Remissions of the pain are less common than with primary ulcer. Weight is lost and the patient is again a dyspeptic invalid usually worse than before his first operation—worried by problems of diet and medicine, frequently off work, irritable and lethargic.

Most of these patients, I believe, take the view that surgery has failed them and that they must be content with the small comfort that diet and medicine will give. A minority, compelled by the severity of their complaint or more often by a complication such as hæmorrhage, perforation or fistula formation, eventually return to hospital. When the patient is examined, the presence of some such complication may be obvious and the investigation and treatment of the case will have to be modified accordingly, as we shall discuss later. In the patient in whom there is no urgent or presenting complication, on the other hand, there may be little objective evidence of the lesion. The story such as we have described is confirmed by the presence of an epigastric scar and some tenderness above the umbilicus or more to the left side. Rarely a mass will be felt. Some features of the changes in symptomatology may point to the fact that we are dealing with a new ulcer in a new situation, but sometimes the diagnosis between recurrent ulceration in the old site and secondary ulceration at the stoma is difficult. We enlist the aid of the radiologist but he cannot promise us a definite answer because stomal and jejunal ulcers are difficult to demonstrate by barium meal. A competent radiologist, however, will give us positive information in about three cases out of four. In the still doubtful cases, gastroscopy has been employed by some to make the diagnosis, but it is questionable if this measure is justifiable. The diagnosis being made on the clinical evidences alone, or corroborated by barium meal X-ray, we must decide what treatment is to be advised.

With this general picture of the disease in our minds we can turn to consider more closely some of the problems raised. In an attempt to probe these I have studied some of the copious literature on the subject and shall necessarily make frequent references to these sources of information. I have also examined the case records of 67 patients with anastomotic ulcers. Some of these were treated by the late Sir David Wilkie, and others were, or now are, under the care of Mr J. M. Graham or Professor J. R. Learmonth, to whom I am indebted for kind permission to use their cases. Because adequate



follow-up of these cases has not yet been possible they provide little statistical information of value, but some interesting facts emerge from their analysis and some individual cases serve to illustrate aspects of the subject.

### PATHOLOGY

It is generally believed that Paterson was right when he said that some of these secondary ulcers develop at the line of anastomosis and that others are strictly jejunal. Strangely enough two of the greatest authorities disagree with this view and with each other. Walton in 1930 wrote: "I believe this distinction (*i.e.* between gastro-jejunal and jejunal ulcers) to be fallacious, for, in every case that I have had the opportunity of examining, the ulcer—even when apparently remote—was connected by a scar with the anastomotic opening and had therefore probably commenced in that situation."

Balfour and Eusterman of the Mayo Clinic, on the other hand, wrote in 1935: "Our experience shows that the great majority of such lesions begin in the jejunum, although they may then attain sufficient size to involve the anastomosis and even in rare instances to extend on the gastric side of the anastomosis."

I suspect that Balfour and Eusterman were influenced by their knowledge of the experimental work of Mann and Williamson in producing jejunal ulcers. Be that as it may, it appears that the fully developed ulcers are in fact found at the anastomosis in about a third of the cases and in the jejunum in the remainder. The anastomotic ulcer may be anywhere on the ring of junction of stomach and jejunum, but is usually at one or other angle. Sometimes there are ulcers at both ends and sometimes ulceration extends round the whole ring. When an anastomotic ulcer is carefully examined after operative resection or at autopsy, it is often found to be on one or other side of the actual line of junction and to be strictly limited by this as a margin.

The great majority of the jejunal ulcers are in the efferent loop within about 2 in. of the anastomosis. Rarely the ulcer is in the afferent loop or on the mesenteric border directly opposite the stoma. Ulcers more than 2 in. from the stoma are rare and when they do occur would appear to be determined in their location by a traumatic factor. In one of our cases a jejunal ulcer formed more than 6 in. from the stoma apparently because there had been a repair of jejunum at the site where the ulcer arose.

These ulcers are in character identical with peptic ulcers elsewhere. Acute varieties are shallow with irregular margins and little induration; these shallow ulcers may have a sloughing base, and hæmorrhage from them is comparatively common and may be severe. Chronic ulcers become deep and indurated and tend in time to penetrate the bowel wall. They may thus cause free perforation into the peritoneal cavity or they may penetrate into adjacent structures and form abscesses, as in the mesocolon (the usual site), the lesser sac of peritoneum, the

liver or the abdominal wall. In a proportion of cases perforation eventually occurs into the transverse colon with the formation of a gastro-jejuno-colic or jejuno-colic fistula. When a chronic stomal ulcer leads to much scarring with or without healing, stenosis of the opening may result. Very rarely a carcinoma develops at the stoma and may surround it: it has been claimed (Konjetzny) that this is secondary to local inflammation, but the development is so infrequent that it may be due to coincidence.

### INCIDENCE

Regarding the incidence of gastro-jejunal ulceration we may note first that, for all practical purposes, it does not occur after gastro-enterostomy or gastrectomy for cancer. I can find in the literature only the following three references to cases of this kind. Paterson quotes a case reported by Einar Key; a woman of 25 years had a partial gastrectomy performed for carcinoma of the stomach, and ten days later the patient died from perforation of ulcers in the afferent loop of jejunum. Evidence that the condition was really carcinoma is missing, and the multiplicity, situation and rapid perforation of the ulcers may lead us to doubt that they were of the "peptic" variety. Another case was reported by Judd in 1921 in the bare words, "one case has been observed in the Mayo Clinic following resection of the stomach for cancer." I have been unable to find any further reference to this case in subsequent reviews emanating from the Mayo Clinic. Horsley, discussing a paper by Dragstedt, referred to "an interesting case reported by Dr Fordyce B. St John of New York; he removed a cancer of the stomach and did a Bilioth II type of operation. Later the patient died from a jejunal ulcer."

Our further considerations therefore will deal only with the incidence of stomal ulceration following operations for peptic ulcer.

It is found that the great majority of those gastro-jejunal ulcers develop between the ages of 30 and 50 years. At the extremes we have the case reported by Mikulicz of a child of 2 months who died from jejunal ulceration, following gastro-enterostomy for congenital pyloric stenosis, and a patient of 81 years described by Hurst.

It is agreed also that the incidence is strikingly higher in men than in women. This difference is more marked than the related sex incidence in duodenal ulcer. Garnett Wright found that in cases of secondary ulceration after gastro-enterostomy for duodenal ulcer the proportion of men to women was approximately 20 to 1. Even after operations for gastric ulcer, in which there is not the same initial difference of incidence, there were more than three times as many men with the complication. In the present series there are 63 men and 4 women, and it is notable that all 15 patients with gastro-jejuno-colic fistula were men. Other reports agree that fistula formation is very rare, though not unknown, in women.

Approximately two-thirds of all cases of secondary ulceration produce symptoms within two years of the first operation. A certain number are never well after the gastro-enterostomy, and others are symptom free for twenty years or more. One patient in the present series developed a gastro-jejuno-colic fistula after being perfectly well for twenty-one years following gastro-enterostomy.

There is evidence that gastro-jejunal ulceration is relatively more common after operations for duodenal ulcer than after operations for gastric ulcer. In the present group of 67 patients only four had their original gastro-enterostomies made for gastric ulcer, while one other had both gastric and duodenal ulcers when first treated. This issue has, however, lost some of its practical importance because of the generally accepted opinion that gastro-enterostomy for gastric ulcer is in any case undesirable in view of the risks of malignancy and the higher proportion of failures to relieve the symptoms due to the primary ulcer.

When we search the literature for statistical comparison of the results of gastro-enterostomy for duodenal ulcer with and without stenosis we get little satisfaction. Opinions are abundant that the incidence of secondary ulceration is higher in the latter case, but evidence is scanty. Douglas (1947) has recently investigated cases at Hammersmith and finds that after operation for duodenal ulcer without stenosis the incidence was 33 per cent. while after operation for duodenal ulcer with stenosis it was only 2.6 per cent.

Before turning to some of the important estimates of the incidence of stomal ulceration that are found in surgical literature, we may profitably consider the criteria on which we must estimate the significance and value of any report.

In the first place we wish to be assured that the series reported was unselected, or at least, to know what factors forced some degree of selection on the writer.

Secondly we wish to know what proportion of cases were traced. Garnett Wright expresses the view that the incidence of secondary ulcer in the untraced group (which constituted one-third in his figures) is less than in those traced because he believed that most patients return to the same surgeon when symptoms recur. This dangerous assumption is opposed by Ogilvie, with good reason, in the words "the jejunal ulcer patient places the greatest possible distance between himself and his first surgeon." The most concrete evidence that these patients do not usually return to their original surgeon is found in a reverse approach to the problem. Walton states that only two in every five patients on whom he operated for stomal ulceration were his own. The Mayo Clinic treated equal numbers from their own clinic and from elsewhere. It follows that we must consider any estimate valuable in proportion to the success of the follow-up and likely to be too low if there are many untraced cases.

Thirdly we wish to know the period of follow-up. Walton, whose

estimate of the incidence is one of the lowest, had to raise his figure from 1·7 to nearly 4 per cent. when he followed a group of cases for ten years or more. It is doubtless true that in about two-thirds of these patients symptoms of gastro-jejunal ulceration start within two years of the first operation, but it must be emphasised that this is a retrospective calculation. In the present series 42 out of 67 patients had symptoms within two years, but in only 34 out of 67 was the diagnosis of gastro-jejunal ulcer made within five years.

Fourthly we must know the criteria on which the diagnosis was based. Hurst rejects Balfour's low estimate of 3 to 4 per cent. as "quite fallacious" because, he says, it was arrived at "by comparing the number of gastro-enterostomies done with the number of gastro-jejunal ulcers returning." We have seen that the victims of this complication probably do not return. Moreover the number of patients reaching any hospital is misleading for another reason, as I have already suggested, namely that, having submitted themselves once unsuccessfully to the surgeon's knife, they will usually—wisely or not—avoid it again. This is strikingly shown in the present series by the observation that, of the 67 patients diagnosed as gastro-jejunal ulcer cases, over 75 per cent. had returned to hospital only because of the compulsion of a serious complication—15 with gastro-jejuno-colic fistula, 18 with perforation and 19 with severe or moderately severe hæmorrhage. It is surely very unlikely that this proportion of all cases of gastro-jejunal ulcer suffer from such complications. It is notoriously the case also that radiological demonstration of gastro-jejunal ulceration is difficult, and even if we allow that over 75 per cent. will be proved by an expert radiologist, an estimate based on this criterion will be too low and a small proportion will be diagnosed only by careful personal examination of the patient.

Investigation of the literature with these requirements in mind will inevitably lead us to the conclusion that no single estimate of the incidence of gastro-jejunal ulcer is entirely reliable and no two estimates are strictly comparable. Nothing is further from my mind than to suggest that any one estimate is valueless. I wish only to insist that each must be judged on its merits.

The reports of most interest to us are those dealing with the incidence of gastro-jejunal ulcer after operations for duodenal ulcer. We find that Walton finally arrived at an estimate of 3·24 per cent. on all cases and 3·97 per cent. on cases followed up for 10 years. This, however, is the personal series of an inevitably biased, however honest, observer, and he had already imposed a selection in the strict application of his own criteria for the operation. Balfour agrees with Walton's figure "when gastro-enterostomy is performed according to the principles as set down elsewhere." "Elsewhere" we find that his principles were very definite—"it is particularly important to avoid the operation if the patient is young, the stomach small, the lesion not extensive and acidity of the gastric content high." This

proviso seems to me to be a very significant qualification which should be, but seldom is, applied to Balfour's much quoted estimate.

Garnett Wright in his collective inquiry arrived at an incidence of 8.75 per cent., but he was apparently relying largely on answers to questionnaires from surgeons who were judging their own cases, and 1 in 3 of the cases was untraced. Ogilvie's figure of 20 per cent. was an estimate based on information and impressions, and though interesting is not admissible as evidence. Lewisohn's figure of 34 per cent. is open to criticism in that he failed to trace about half of his patients in spite of an exhaustive search. On the other hand his personal examination and criteria for diagnosis are impressive. Douglas's recent investigation was more successful in the number traced and equally thorough in respect of diagnosis: it revealed an incidence of 18 per cent. in all cases of duodenal ulcer and 33 per cent. in cases of duodenal ulcer without stenosis. The figure of 73 per cent. given by Hurst and Stewart is based on autopsy material and is therefore, as they admit, too high. If, however, their method of selection can be evaluated their diagnosis is incontrovertible!

I fear that, like myself, you will be only the more confused by this recital of figures and pros and cons. My own conclusions from the evidence would be that if cases are carefully selected as suitable for the operation of gastro-enterostomy, the incidence of gastro-jejunal ulcer should be less than 3 per cent. If gastro-enterostomy is performed for all cases of duodenal ulcer, irrespective of sex, age or the degree of stenosis or hyperacidity, the incidence of gastro-jejunal ulcer will be 20 per cent. or more.

As to the incidence of gastro-jejunal ulcer after partial gastrectomy, it is clear that the complication is relatively rare and most authorities are agreed that it is under 2 per cent. Several higher estimates are vitiated from our point of view because they include cases of gastro-jejunal ulcer that followed what we now consider to be an inadequate gastric resection for cases of ulcer with high acidity. This is borne out by the result given by Garnett Wright. After 633 cases of partial gastrectomy of the Polya type for ulcer, the incidence of anastomotic ulceration was less than 1 per cent. After 123 cases of partial gastrectomy by the Bilroth I method there was stomal ulceration in 9 per cent. In the continental journals, there have recently been reports of gastro-jejunal ulcer following gastrectomy, but when we find that these are reports of small series of collected cases like 6 or 9 and when we reflect how prevalent the operation of partial gastrectomy has been on the Continent for many years, it does not appear that the incidence is high or even rising with time.

#### PATHOGENESIS

The fundamental cause of gastro-jejunal ulceration is the same as that of peptic ulcer elsewhere—if we but knew it. I do not propose to venture on that unsolved problem now, but some factors relating particularly to gastro-jejunal ulceration may be mentioned.



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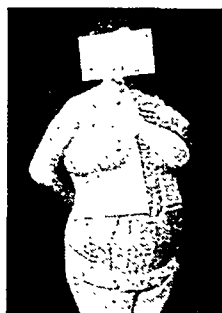
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It has long been believed that the actual technique of the surgeon in making the gastro-enterostomy opening plays a part. It is doubtless true that any error in positioning of the stoma or the jejunum which results in a partial obstruction in the region of the outlet may interfere with the neutralisation of gastric chyme before or as it enters the jejunum, and so dispose to ulceration. But apart from such a technical fault the only things that can be considered to be established both clinically and experimentally are : (1) that the more distal the portion of jejunum involved in the anastomosis, the greater the liability to ulcer ; (2) that any procedure that deflects the alkaline duodenal secretions from the area of the anastomosis disposes to ulceration.

It is agreed, therefore, that the proximal loop of jejunum should be as short as is mechanically convenient, and that procedures like the making of an anastomosis between afferent and efferent loops or the anastomosis " en Y " of Roux are to be avoided.

It has been suggested also that the use of clamps during the operation traumatises the mucosa and leaves a devitalised area on which the acid chyme can work ; that the use of unabsorbable sutures on the mucosal aspect prevents complete healing or that imperfect hæmostasis at the suture line leaves a hæmatoma which makes an area of weakened resistance.

All these may on occasion play a part. Doubtless when the ulcer diathesis and the acid chyme are present an injured area may determine the site of an ulcer ; but these traumatic factors must be present in many of the patients who develop no secondary ulcer and in many of the anastomoses performed in operations for cancer. If the use of clamps or of non-absorbable sutures was a significant factor, some of the many workers who have sought statistical evidence of their rôle would have found it by now ; in fact there is no such evidence.

Do the observed facts of gastro-jejunal ulceration shed any light on the general problem of the aetiology of peptic ulcer ? The observation that ulcer does not follow operations for carcinoma of the stomach strikes us immediately as significant. This might be due to the fact that these patients do not on the average live long enough to show signs of stomal ulceration—but many of them live as long as the two years that cover the appearance of the majority of secondary ulcers in the ulcer cases. We must ascribe the absence then to the fact that 60 per cent. of patients with stomach cancer have achlorhydria and the remainder have a low or normal acidity. Many writers, such as Walton, Hurst, Lewisohn and Douglas, have adduced other evidence that there is correlation between the degree of acidity and the incidence of stomal ulcer. We are now finding further confirmation of the importance of the acid level in the observation that the few patients who develop gastro-jejunal ulceration after partial gastrectomy are all apparently in the group in whom removal of as much as three-quarters of the stomach does not significantly lower the hydrochloric acid concentration.



I do not think it can be said that study of these cases of gastro-jejunal ulceration sheds any great light on the problem of the ulcer diathesis, but it does provide us with the most vivid pictures of the diathesis at work. In the present series, 13 of the 67 patients have had repeated operations for anastomotic ulceration, and the follow-up records at present available show that many others relapsed after conservative operative measures.

Three cases from Sir David Wilkie's records are of special interest because they are striking examples of recurrent ulceration after repeated operations and because they were finally treated by partial gastrectomy more than ten years ago. They are the only patients (in the group I have reviewed) on whom Sir David Wilkie performed gastrectomy.

T. F. had a gastro-enterostomy performed after hæmatemesis and perforation of a duodenal ulcer. Gastro-jejunal ulceration with hæmorrhage followed and the anastomosis was undone. Recurrence of duodenal ulceration with evidence of duodenal ileus led to gastro-duodenostomy and duodeno-jejunosomy. Severe ulceration occurred at the new stoma and in 1937 a partial gastrectomy was performed.

D. M. had a gastro-enterostomy for duodenal ulcer but stomal ulceration followed and later the anastomosis was undone and a gastro-duodenostomy made. This became stenosed by chronic ulceration and a new gastro-enterostomy was required. Again gastro-jejunal ulceration occurred, and in 1935 a partial gastrectomy was performed.

J. G. had a gastro-enterostomy for duodenal ulcer followed by secondary ulcers at the stoma. The anastomosis was undone and a gastro-duodenostomy was made, again with stomal ulceration. A new gastro-enterostomy was tried with the same result. Finally in 1935 a partial gastrectomy was performed.

The most instructive feature of these cases is this: that recent follow-up shows that since gastrectomy all three have remained well and regularly at work until 1947.

### TREATMENT

Preventive treatment of gastro-jejunal ulcer must consist primarily in the careful selection of cases for the operation of gastro-jejunosomy. Such stories as those I have just told may leave us with some sympathy with the dictum, "Gastro-enterostomy is not a treatment, it is a disease," but it is not so. It is a comparatively simple operation with a low mortality and it will give complete relief to many sufferers. The difficulty is to choose the right cases. In the present state of our knowledge it is probably wise to avoid the operation in any patient under 45 years of age unless there are contra-indications to the more formidable procedure of partial gastrectomy; and to confine its use to patients in whom the peptic ulcer is associated with some degree of pyloric stenosis and a normal or low acid curve.

The precept to avoid gastro-enterostomy where the fractional test meal shows a high free acid is unfortunately more theoretical

than practical because the significant acid level is that which will occur *after* the gastro-enterostomy has been established, when the associated relief of gastritis often results in a considerable increase in acid secretion.

When the operation is done it must be regarded only as an incident in the medical treatment of the case. Preparation for operation should include the eradication of all foci of sepsis and every possible measure such as change of occupation to relieve mental strain and worry. After operation diet must be continued, smoking must be reduced, alcohol and spices avoided, and suitable alkalis taken regularly.

The treatment of an established gastro-jejunal ulcer raises other problems. In early or mild cases medical measures should be tried and may give relief, but if they are not quickly and completely successful they should not, I believe, be continued to the exclusion of surgery. It is probable that few gastro-jejunal ulcers, once chronic, really heal; and the patient who is kept just barely comfortable by diet and alkalis may be slowly but surely developing further trouble at his anastomosis. The complications of gastro-jejunal ulcer, as we have seen, are relatively frequent and serious. Even if perforation, hæmorrhage or fistula does not ensue, every month of delay may let a chronic ulcer build up a greater mass of fibrotic tissue with œdema and adhesions, and the subsequent operation becomes more difficult and dangerous. This inflammatory mass is generally situated in the mesocolon and the surgeon will have to dissect it laboriously from vital structures—the pancreas, the middle colic artery, and the colon itself. In most cases the only cure is by surgical treatment, and the sooner the better.

Numerous operative measures have been tried: reconstitution of the normal by undoing the gastro-enterostomy was for a time accepted as the obvious solution, but there are many overwhelming objections to this both in theory and in practice. It is not applicable to cases with pyloric stenosis, and in cases without pyloric stenosis it will be followed almost certainly by reactivation of the primary ulcer. It involves the most difficult and dangerous part of any operative procedure—the dissection of the ulcer area and the reconstitution of the jejunum. In practice it has been found to have an operative mortality rate of no less than 12 per cent.

Local measures to excise or cauterise the ulcer have also been tried without success; recurrence follows in a majority of cases.

Undoing the gastro-enterostomy along with gastro-duodenostomy or pyloroplasty was popular for a time, but has not proved satisfactory. The three case histories I have recounted illustrate the usual result. In the present series 8 out of the 12 cases treated by gastro-duodenostomy are known to have shown definitely unsatisfactory results, and the proportion may be higher as the remaining 4 have not yet been traced.

The formation of a new gastro-enterostomy has also proved in-

effective. In 55 cases recorded by Garnett Wright the operative mortality was 16 per cent. and the percentage of good ultimate results was only 20.

Partial gastrectomy has been proved by experience to be a satisfactory treatment of gastro-jejunal ulceration. In practice it produces a high percentage of cures. The operative mortality of partial gastrectomy for anastomotic ulcer has, however, been unfortunately high. In Garnett Wright's figures it was about 12 per cent. for all types of gastrectomy, but higher—about 15 per cent.—for the more radical excisions such as are now believed to be desirable to cure the condition. It will be observed that the higher figure (15 per cent.) is no greater than the mortality quoted for some conservative operative procedures. That this mortality can and should be reduced there is no doubt. That it can be reduced is shown by the Mayo Clinic reports of 89 consecutive cases of partial gastrectomy for gastro-jejunal ulceration with a mortality of 3.37 per cent. That it will be reduced even in the average surgical clinic is a belief I would support with several arguments. Surgeons in this country were slow to adopt the radical measure of partial gastrectomy, and until quite recently comparatively few had sufficient experience to be technically expert in the procedure. Even more important, however, are concomitant advances in anæsthesia and in pre-operative and post-operative treatment. The introduction of methods of anæsthesia, as with cyclopropane and curare, which are non-toxic, removed much of the danger of an operation which may last two hours or more. The patient can be made fit for operation by high-protein high-carbohydrate diet and blood transfusion if necessary. The dangers of operative shock are greatly reduced by the extended use of intravenous blood and plasma. Infective complications are countered as never before by penicillin and the sulphonamides. The dangers of vomiting after operation are avoided by continuous gastric suction, and the patient is kept adequately hydrated and nourished in the post-operative period by intravenous solutions.

Vagotomy is now under trial as an alternative method of reducing the hydrochloric acid secretion. The immediate results of the operation are very gratifying: there is complete relief of ulcer pain and a marked fall in acidity. It is still too early to judge the lasting value of the procedure, but it can on present evidence be regarded as the treatment of choice for anastomotic ulcer in elderly or bad risk patients and in all cases of recurrent ulcer after partial gastrectomy.

#### COMPLICATIONS OF GASTRO-JEJUNAL ULCERATION

It remains to consider some of the important complications of gastro-jejunal ulcers and their treatment.

The development of an *abscess in the anterior abdominal wall* was previously a common event in these cases, but is now rarely seen,

because the anterior anastomosis is seldom performed. The greatest danger of such an abscess lies in the fact that if it bursts or is incised a fistula communicating with the jejunum is liable to be formed—an event to be guarded against if at all possible.

*Free perforation* into the peritoneal cavity is, as we have seen, comparatively common. In the present series it occurred in 18 of the 67 patients. It may occur repeatedly as in one of our patients who had three stomal perforations before partial gastrectomy was successfully performed. Perforation is usually to be taken as an indication to treat the patient by gastrectomy as soon as he has recovered sufficiently from the primary operation for closure.

The clinical picture in these cases is almost identical with that of perforation of a primary peptic ulcer though the correct diagnosis may be made from a knowledge of the history, and interpretation of unusual distribution of maximal tenderness and rigidity. At operation in these cases the perforation may be difficult to find owing to numerous adhesions and to its deep situation. When found it may also be difficult to close, and no attempt should be made to excise or invaginate an ulcer near the stoma. It is quite sufficient to suture a tag of omentum over the hole.

*Hæmorrhage* from a gastro-jejunal ulcer presents considerable difficulty both in diagnosis and in treatment. The diagnostic problem is to decide whether the hæmorrhage is from a stomal ulcer or from a recrudescence of the primary ulcer. Fortunately, hæmorrhage from a secondary ulcer is seldom so severe or persistent as may be the case when a posterior duodenal ulcer erodes a branch of the gastro-duodenal artery.

The difficulties of these cases are well illustrated by the following history :—

A. S. had a gastro-enterostomy made for duodenal ulcer in 1936 when he was 30 years old. He continued to have symptoms and in 1945 had a second operation for severe and recurrent hæmatemesis. He was admitted to our wards in February 1946 with persistent hæmorrhage. It was appreciated that this bleeding might be from a stomal ulcer but in view of its severity and constant severe pain boring through to the back it was judged that it probably came from a penetrating posterior duodenal ulcer. Professor Learmonth operated on him and found neither a bleeding point in the duodenum nor a palpable ulcer at the anastomosis. He opened the anterior wall of the stomach and, examining the stoma from within, found a large shallow ulcer extending into the efferent jejunal loop. Hæmorrhage from such an ulcer can be treated only by a wide resection, and the patient was not fit for such a procedure. The stomach and abdomen were closed and blood transfusion continued. Fortunately bleeding stopped spontaneously and Professor Learmonth was later able to perform a partial (three-quarters) gastrectomy. The patient remained well for a year but then developed an ulcer at the new anastomosis. He has now been relieved by vagotomy.

The last complication is that of *gastro-jejuno-colic fistula*—one of

the most interesting and difficult problems that can confront an abdominal surgeon.

The symptoms are very characteristic—diarrhœa, vomiting of fæcal material, belching of foul gas and progressive wasting. Pain is frequently absent or slight. Hurst believes that fistula often results from the invasion of an acute ulcer and this may explain the absence of preceding pain in some cases. There is no doubt that the actual ulceration often heals after the formation of a fistula, and this may be the explanation of the infrequency of pain in the symptom complex of the developed condition.

One or more of the classical symptoms are absent in some cases ; the most constant feature is severe diarrhœa. It is usually said that the condition is rapidly progressive with extreme wasting and is inevitably fatal, but this is not always true. The symptoms are sometimes intermittent and though most cases show loss of weight and some show rapid and extreme wasting, with signs of gross protein deficiency, a few are more inconvenienced than ill. We have recently had a patient who had the unmistakable symptoms of gastro-colic fistula for a period of one to two weeks once a year for seven years. Between these attacks his health was good. A barium enema demonstrated the fistula and precipitated a short attack of severe diarrhœa and fæcal vomiting.

The cause of the diarrhœa in these patients is an interesting problem with an important bearing on the treatment. It was formerly assumed that the diarrhœa was due to acid gastric content entering the colon. That this is probably incorrect is suggested by the infrequency with which totally undigested food is recognised in the stool and by the fact that a barium meal fails in a high proportion of cases to demonstrate the fistula. In 9 of the 15 patients in this series both barium meal and barium enema X-ray examinations were carried out and in 6 of these the meal failed to demonstrate the fistula ; the enema showed the fistula in all 9. It must be concluded that the severe diarrhœa which characterises these cases is really a small intestine diarrhœa due to irritation of the jejunum by the contents of the colon. This view serves also to explain the rapid dehydration and starvation of those patients in whom the diarrhœa is not intermittent. It is confirmed also by experience in the treatment of these cases, as I shall describe later.

Gastro-jejuno-colic fistula is an extremely grave condition. If untreated it will cause death more or less rapidly in a large majority of cases and until recently the mortality of surgical treatment was generally over 50 per cent. The great obstacles to any operative procedure are the poor general condition of all the tissues in the region of the fistula, and the fact that operation must include repair or resection of the colon with all its attendant dangers. Some two-stage procedure is usually necessary.

Various alternatives have been suggested. Lahey and Marshall

have advised a preliminary ileo-sigmoidostomy followed by resection of the right colon from the cæcum to the splenic flexure, and partial gastrectomy. This seems an unnecessarily formidable procedure.

Wilkie proposed, and employed with some success, a simple manœuvre by which he isolated and closed the segment of the transverse colon including the fistula, and reconstituted the colon by end-to-end anastomosis. This has the advantage that in a patient in whom the more serious undertaking of partial gastrectomy is contra-indicated the one operation may be sufficient, but without a second stage operation it may prove less radical than is required in such cases. One of our patients had a recurrence of fistula seven years after this procedure was carried out.

A simpler and completely effective first stage was first proposed by Pfeiffer who mobilised the ascending colon and made a double-barrelled colostomy on the right side. There are many disadvantages and no important advantages in using the ascending colon, and a colostomy made from the proximal part of the transverse colon is technically simpler and equally effective. This is the method which I have learned from Mr J. M. Graham and Professor J. R. Learmonth, in whose cases I have now seen it used repeatedly with striking success. In every case the vomiting and diarrhœa have stopped completely from the moment the proximal transverse colostomy was made. It is this dramatic relief which provides the final proof that the diarrhœa in these patients is due to colonic contents entering and irritating the small intestine. The colostomy motions are loose for a day or two but soon become reasonably firm. The patient gains weight and strength rapidly and is soon fit for the second stage.

When partial gastrectomy is now undertaken it is found that inflammation in the area of the fistula has resolved; the operation can be carried out with comparative ease and safety. The transverse colostomy is closed later.

This procedure has recently been carried out in 6 patients in Professor Learmonth's Unit. There have been two deaths, both due to late complications not directly related to the disease or operation. One of the four patients successfully treated was a man with complete heart block and severe chronic bronchitis.

### CONCLUSION

Such an account as I have tried to give of gastro-jejunal ulcer and its complications is in many ways a sad story of the depressing results of surgical failure. The disease itself has in the past been the cause of death in more than 1 in 4 of its victims. But I hope that I have also been able to show you the rays of hope; that, learning by our past mistakes, we should be able almost completely, if not completely, to prevent its further occurrence; and that, by modern surgical measures, we should be able to reduce considerably both its morbidity

and its mortality. It remains now to find a method other than gastrectomy that will effect lasting reduction of the hydrochloric acid secretion, so that we may aspire to relieve the unfortunate patient of his ulcer but leave him his stomach.

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# PARTIAL GASTRECTOMY FOR PEPTIC ULCER

By H. W. PORTER

WHILE the final answer to the treatment of chronic peptic ulceration will almost certainly be found in the sphere of the physician, there is at present a considerable proportion of cases who can obtain no permanent alleviation of symptoms from medical treatment<sup>1, 2</sup> and the majority of these can be greatly benefited, if not completely relieved, by the surgeon.

It is not intended in this paper to discuss the many forms of surgical treatment but merely the operation of sub-total gastrectomy. The aim of this operation is to remove the part of the stomach which is concerned with the hormonal phase of digestion, and at the same time, in the great majority of gastrectomies, to defunction the first part of the duodenum completely.

In order to make certain of an adequate reduction in acidity, it was conclusively shown by Lorenz and Scheer<sup>3</sup> in 1922, and by many workers since,<sup>4</sup> that although gastrin is secreted in the pyloric antrum, pylorotomy alone is not sufficient, and at least two-thirds or three-quarters of the stomach must be removed.

This operation of partial gastrectomy has on the whole given the most consistently good results, although it has, like any operation, its disadvantages.

The disadvantages of partial gastrectomy may be tabulated under the following headings :—

- (1) The operative mortality.
- (2) Anastomotic ulcer.
- (3) Inability to return to normal diet.
- (4) Post-operative dumping syndrome.
- (5) Anæmia.
- (6) Inability to return to former employment.

The observations in this series are based on an analysis of 118 unselected cases. There have been 87 duodenal ulcers, 20 gastric ulcers, and 11 stomal ulcers.

The age incidence is seen in Table I :—

TABLE I					
<i>Age Groups</i>					
20-30	30-40	40-50	50-60	60-70	Total
7	33	49	23	6	118

A Honyman Gillespie Lecture delivered in the Royal Infirmary, 27th May 1948.

The indications for operation have been :—

TABLE II

<i>Repeated perforations</i> —1	.	.	.	30 cases	
" " 2	.	.	.	7 "	
" " 4	.	.	.	1 "	
				<hr/>	38
<i>Hæmorrhage</i> —Acute massive	.	.	.	8 cases	
" Multiple	.	.	.	9 "	
				<hr/>	17
<i>Failed medical treatment</i>	.	.	.	.	63
					<hr/>
					118

It is exceedingly difficult to dogmatise on what constitutes "failed medical treatment," but I believe that the following may be taken as a guide :—

- (a) A patient who has had more than one adequate course of medical treatment in hospital and who fails to respond or has a recurrence in spite of adhering to medical treatment after discharge.
- (b) People who are unable to continue adequate medical treatment due either to economic factors or low intelligence.

With few exceptions, the cases in this group have been transferred from medical wards.

Some of the cases have been complicated and surgery has not been denied to patients because of associated pathology. Patients who were also suffering from the following have been operated on :—

TABLE III

Chronic bronchitis or asthma	.	.	.	.	.	6
Bronchiectasis	.	.	.	.	.	2
Cardio-vascular disease	.	.	.	.	.	6
Severe alcoholism	.	.	.	.	.	1
Syphilis	.	.	.	.	.	1
					<hr/>	
						16

I believe that the type of operation carried out has a considerable influence on the end results, and I intend to discuss the technique of the operation which I have carried out in this series in some detail, giving the reasons for the various steps of the operation. Although this is a comparatively small series of cases, I think that the conclusions which may be drawn from the results are of some value as the technique used has been virtually the same in every case.

#### PRE-OPERATIVE TREATMENT

In the uncomplicated case, the patient is admitted to hospital two days before operation. He is given a cathartic that night, and the following day has a low residue light diet. In the evening he has

gr. iii soneryl, and on the morning of operation his stomach is washed out, the gastric tube being withdrawn after the lavage.

Pre-medication is given three-quarters of an hour before operation, and an intravenous drip is instituted.

In cases where there has been gross upset in blood chemistry as a result of vomiting from pyloric obstruction, water salt balance is corrected before operation.

Where there has been pre-operative hæmorrhage, the anæmia is corrected as far as possible before operation and blood is given throughout.

Blood is not given in the straightforward case unless specially indicated.

### ANÆSTHETIC

There can be little doubt that one of the factors which has been responsible in reducing the mortality and incidence of post-operative complications has been the recent advance in anæsthesia, and I should like to acknowledge the debt which I owe to our anæsthetist for her co-operation and skill in dealing with these cases. The majority have been induced with pentothal and this has been followed by cyclopropane and more recently with curare in addition.

### OPERATION

A right upper paramedian incision is made, the anterior rectus sheath is incised and the rectus muscle reflected laterally before opening the posterior rectus sheath and peritoneum in the line of the original incision. This takes very little extra time and makes for a much safer and firmer closure of the wound. With this type of incision there has been no case of hernia or weakness in the abdominal wall so far.

After inspecting the stomach and duodenum and having decided to proceed with the gastrectomy, the stomach is mobilised along the greater curvature by dividing the greater omentum between ligatures as far to the left as the gastro-splenic ligament and to the right to the pylorus.

The lesser omentum is then partially mobilised to the right so that the pylorus can be visualised in its entirety.

The first part of the duodenum is then crushed and divided as close to the pylorus as possible and the distal part invaginated. I do not think that there is any optimum method of closure, and that the method must vary with the individual case. Nor is it necessary or advisable always to remove an ulcer in this region if this is going to be hazardous, as when the first part of the duodenum is closed, the ulcer will almost invariably heal.

If there is a large indurated ulcer present, I have on occasion carried out a submucous resection of the antrum and used

the seromuscular layers to complete closure. While this may be justifiable under certain exceptional conditions, it is not without its risks.

While leakage at the duodenal stump is one of the recognised complications of partial gastrectomy, and one of the common causes of mortality, I do not believe that the manner in which closure is made affects leakage materially, provided reasonable care is taken.

It may be that too great mobilisation of the duodenum with occlusion of Wilkie's end artery and resultant ischemia may result in necrosis and leakage. This suggestion is strongly supported by the recent work of Shapiro and Robillard,<sup>5</sup> who show quite conclusively that too great mobilisation of the duodenum may impair its blood supply and is dangerous.

By far the most important factor in duodenal leakage is obstruction to the outflow of duodenal contents, which is normally 1500 c.c. a day, by kinking and/or œdema of the jejunum at the site of the anastomosis.

In this series I have been fortunate in having had no case of leakage at the duodenal stump.

Having dealt with the duodenal stump, the mobilised part of the stomach is then turned upwards towards the left shoulder, and the left gastric vessels are defined and doubly ligated before being divided. Two ligatures are applied as a precautionary measure, as these vessels retract after they are divided, and should a ligature slip there may be considerable hæmorrhage and difficulty in identifying and catching the bleeding point.

Mobilisation now being completed, the transverse colon and meso-colon are delivered from the abdomen, the first loop of jejunum is defined, and after making an incision through the meso-colon to the left of the middle colic artery, the distal three-quarters of the stomach is drawn down through the opening. I do not think that this procedure has been previously described but was taught by my former chief Mr J. M. Graham. The first loop of jejunum is then approximated to the stomach so that the proximal part of this loop lies towards the lesser curvature, in the position in which the completed anastomosis is going to lie, making the jejunal loop as short as possible.

There is considerable difference of opinion as to the value of a short proximal jejunal loop, but if one accepts Wangenstein's<sup>6</sup> experimental work which suggests that a hormone is produced by the entry of food into the duodenum or proximal 2 or 3 inches of the jejunum which, in turn, stimulates the secretion of alkaline, duodenal and pancreatic juices, then it is obviously desirable that the site of anastomosis should be in this area. There is, in addition, considerable clinical evidence to show that the incidence of stomal ulceration is very much less in those cases who have a short proximal loop.<sup>7, 8, 9</sup>

Keiffer<sup>10</sup> found that at the Lahey Clinic there was a 10 per cent. incidence of stomal ulceration following the use of the long anterior loop.

Also it seems probable that a long proximal loop would be more susceptible to distension with resultant dragging and kinking at the anastomotic site, therefore more chance of closed loop obstruction and duodenal stump leakage. Ogilvie<sup>11</sup> has also pointed out that the arteries of the jejunum are only 4 inches long and inelastic, and if there is any tension on them, ischaemia and possibly necrosis may occur at the site of anastomosis.

The main argument expressed in favour of the long anticolic anastomosis, is the somewhat doubtful one that should a stomal ulcer occur, it is more accessible.

Having applied Swanson's gastro-enterostomy clamps and adjusted the parts to be joined so that the jejunum is slightly overlapping the edges of the stomach, a posterior sero-muscular stitch of linen thread is introduced. A non-absorbable suture is used for this layer as it is safer than catgut.

A large Payr's clamp is then applied to the stomach about  $\frac{1}{4}$  inch beyond this suture line and the stomach is cut across proximal to the clamp.

All except the lower  $2\frac{1}{2}$  cms. of the open part of the gastric remnant is then closed by suturing first mucous membrane to mucous membrane and then invaginating this suture line by suturing the anterior and posterior seromuscular layers of the stomach together.

The opening in the jejunum is then made opposite the remaining opening in the stomach and the anastomosis completed using two continuous through-and-through sutures in preference to a Connel stitch which is not so hæmostatic.

Finally, a full length seromuscular linen thread suture is inserted.

It will be noticed that a much smaller stoma than is customary is made and I think this small stoma has certain advantages.

(1) The advantages of a Hoffmeister-Finsterer valve are present. There appears to be some confusion as to what constitutes a Hoffmeister valve, which was first described by Hoffmeister<sup>12</sup> in 1906—this was merely the turning in of the upper 2 cms. or so of the gastric remnant to reduce the chance of leakage at the upper part of the anastomosis. Later, in 1924, Finsterer,<sup>13</sup> believing that discomfort followed the regurgitation of food into the proximal loop, increased the length of this closure in an attempt to form a valve, but he nevertheless made quite a large stoma.

(2) Recently a distressing feature of partial gastrectomy has been recognised, namely the dumping syndrome. Gilbert and Dunlop<sup>14</sup> found that 35 per cent. of patients who had undergone partial gastrectomy for ulcer suffered from these distressing symptoms and a small percentage of their cases were so crippled as to be unfit for any kind of work.

While the cause of dumping is not yet fully understood, all are agreed that the predisposing factor is too rapid emptying of the gastric remnant.

It has also been known for a long time that the symptoms of dumping tend to clear up after months or years, and that even with a full-length anastomosis, dilatation of the gastric remnant may occur and the stoma may take on a sphincteric-like action.

Schindler<sup>15</sup> reported four such cases in a series of 52 who had had a full-length anastomosis made and whom he examined with the gastroscope, and these four patients were the only ones who were entirely symptom free.

There is evidence in this series to show that a sphincteric-like action may occur with the small stoma at a relatively early stage.

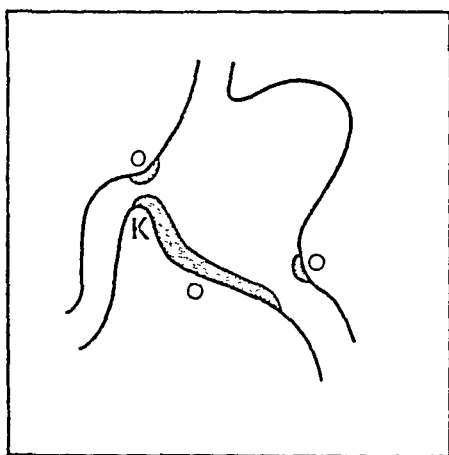


FIG. 1.—Line drawing of full-length stoma after gastrectomy. Note the site of the kink (K) and the stoma where operative œdema may occur are superimposed on one another.

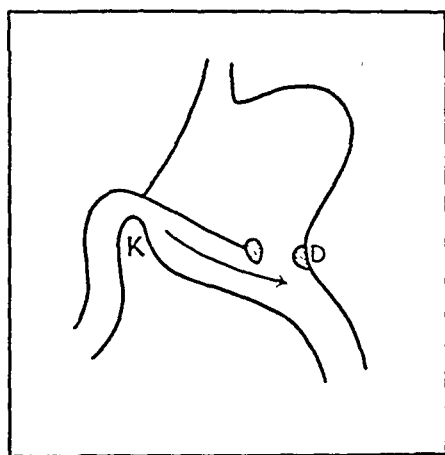


FIG. 2.—Line drawing of small stoma gastrectomy. The sites of the stoma and the kink where obstruction may occur are held widely apart.

(3) The risk of post-operative hæmorrhage is reduced because only a small incision is made in the jejunum.

(4) Should œdema occur at the stoma or in the jejunum, œdema and kinking cannot occur at the same place, with corresponding reduction in the possibility of partial obstruction in the proximal loop and duodenal leakage (Figs. 1 and 2).

(5) Lastly the small stoma appears to favour early dilatation of the gastric remnant, which enables the patient to return to a full normal diet sooner. This not only enables him to regain weight but has a most desirable psychological effect.

Having completed the anastomosis, the stomach is then stitched to the edges of the opening in the meso-colon to prevent the anastomosis retracting upwards, and the wound is closed in layers.

A single strip of elastoplast is applied as a dressing. This does not constrict the patient's abdomen and allows full excursion of the diaphragm.

## POST-OPERATIVE TREATMENT

Following operation, the intravenous drip is continued for twenty-four hours, but in the average case fluids, sweet drinks and milk are started the evening of operation. Fluid by mouth is restricted and gastric suction instituted only in those exceptional cases where there is definite indication that the stoma is not functioning satisfactorily. Gastric suction has been required in 7 cases in the series; in one of these there was an organic small bowel obstruction which necessitated further operation and separation of an adherent loop of small intestine to the inside of the wound; in one case the stoma was made too small, and re-operation and enlargement was required; and in 7 cases there was slight post-operative hæmorrhage causing nausea and sickness. All these cases settled down with conservative treatment.

In the vast majority of cases, no suction is necessary and there is radiological evidence, as well as clinical, to show that the stoma functions from the start (Fig. 3).

I think that the routine use of continuous gastric suction is not only unnecessary but may be harmful, as it makes the patient uncomfortable and hinders free movement and coughing, which is so important at this stage of convalescence.

On the first post-operative day, two-hourly feeds of milk or sweet tea or bovril are given and in the evening a little bread and butter or toast.

The intravenous drip is discontinued in the evening, but should the patient be having much pain, he is given 20 c.c. of 1 per cent. procaine intravenously in it before the needle is withdrawn. This has a marked local anæsthetic effect on the wound and enables the patient to get up into a chair to have his bed made without undue discomfort.

The value of early rising in these cases cannot be over-stressed as the movement and upright sitting position not only encourages full diaphragmatic excursion but also helps the patient to pass flatus, and almost completely eliminates post-operative distension and ileus.

It may also discourage thrombosis and embolus but it is not for this reason that early rising is advised. There has actually been one case of small pulmonary embolus in a patient who had been getting up from the start.

On the second post-operative day, two-hourly feeding is maintained but in addition, a little solid food—steamed fish or chicken may be given.

On the third day a full light diet four-hourly is started. An aperient is given in the morning and he is encouraged to walk.

After this, diet and exercise are gradually increased so that on the fifth day many patients can walk 100 yards and by the twelfth day the uncomplicated case should be able to take a full normal diet and be ready for discharge. Seventy per cent. of cases done since this



regime was started two years ago, have actually left hospital in under fifteen days.

At this stage it is usually necessary to give four meals a day instead of three as the gastric remnant has not yet dilated to its ultimate size.

The patient should be able to return to work on a full normal diet in six to eight weeks after operation.

It is of the utmost importance during the immediate post-operative period to re-educate the patient to consider himself a normal individual with a normal stomach. And it is equally important to explain to the patient before operation the post-operative treatment so that his co-operation may be as complete as possible.

## RESULTS

*Mortality.*—For the purpose of analysing the *mortality* and immediate post-complications, 118 cases are available. There have been four deaths. The first occurred in a man aged 55, who had a very long history—seventeen years—of ulcer, and who had amœbic dysentery in 1916 which had been quiescent since.

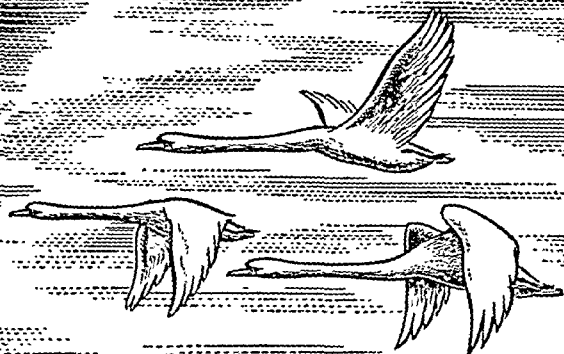
An uneventful gastrectomy was carried out but on the fourth day he began passing blood and mucous, and on the sixth day his cæcum perforated. This was drained and emetin was injected through the cæcostomy, but death occurred on the eleventh day. At post-mortem, the whole mucosa of the colon had sloughed.

The second death occurred in a stout female aged 55, who suffered from chronic bronchitis and myocarditis and who was operated on for a large ventral hernia which was thought to be causing pain and sickness. At operation, however, the stomach which had a very large lesser curvature ulcer of doubtful innocence, was found in the sac, and since it was then obvious to what her symptoms were due, and because of the questionable innocence of the lesion, a partial gastrectomy was carried out and the hernia repaired. This patient began to make a satisfactory recovery but on her twenty-second post-operative day, she developed myocardial failure and died.

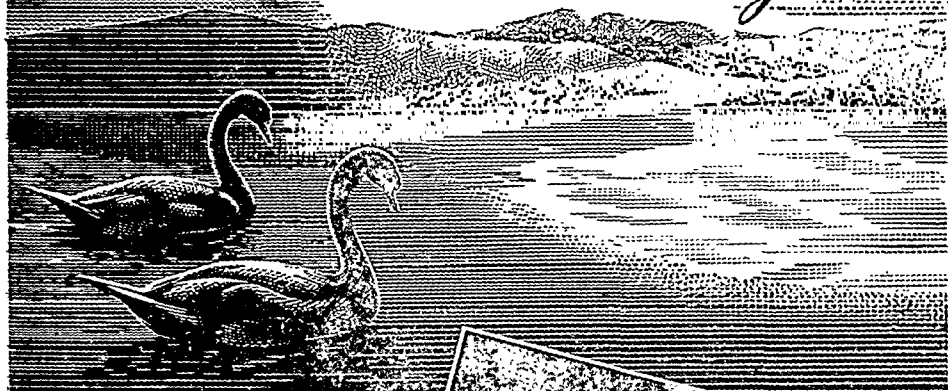
The third death occurred recently in a man of 50, who had an enormous duodenal ulcer with inflammatory stenosis, weighed 6 stones and had a +++ W.R. He unfortunately developed a right lobar pneumonia which failed to respond to penicillin.

The fourth death which also occurred recently was in a man aged 56, who had had one previous perforation and was admitted as a possible leaking perforation. At operation there was no actual peritonitis but a very indurated ulcer. A partial gastrectomy was carried out but the ulcer was left *in situ*—closure being made by Bancroft's method. This man was exceedingly well for two days after which he developed signs of peritonitis and it was thought that the closed stump must have necrosed and leaked. His abdomen was drained, but unfortunately, he died, and at post-mortem it was found that the stump was intact.

*calm  
sleep*



*— and bright  
awakening*



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It will be noticed that all these deaths occurred in patients in the 50-60 age group, which may be an argument for instituting surgical treatment at an earlier date.

TABLE IV

*Post-Operative Complications*

Pulmonary atelectasis	. . . . . 22	19 per cent.
Hæmorrhage . . . . .	7	6 "
Pulmonary embolus . . . . .	1	1 "
Pneumothorax . . . . .	1	1 "
Obstruction at stoma . . . . .	1	1 "
Bowel obstruction . . . . .	1	1 "
Leakage from duodenal stump . . . . .	0	0 "

It will be noticed that by far the most serious complications with which we have had to deal are those affecting the respiratory system. Nineteen per cent., it will be noted, suffered from pulmonary atelectasis. While this may appear to be a very high figure, it compares favourably with figures quoted in the literature by other observers; for instance Minnipress and Etheridge<sup>16</sup> reported 30 per cent. incidence in a series of 100 cases.

The majority of these cases of pulmonary collapse have been of a minor degree and I have included as cases of atelectasis all those patients who have had a rise in temperature of 100° F. associated with slight cough and later some muco-purulent sputum.

With the exception of the case of lobar pneumonia who died, all have made a satisfactory recovery. There are several factors which I think are worthy of consideration in this respect.

## (1) Prophylactically:—

- (a) The abolition of constricting abdominal binders and dressings.
- (b) Early rising to encourage abdominal breathing.
- (c) The avoidance of indiscriminate use of gastric suction.
- (d) Encouragement to cough. This not only entails reassuring the patient regarding the ability of his wound to stand strain of coughing, but may also necessitate personal supervision to make sure that he does cough.
- (e) The avoidance of respiratory depressant drugs as far as possible, especially morphia, and I think that the use of intravenous procaine may prove itself to be a suitable substitute.
- (f) The avoidance of post-operative dehydration.

(2) In the treatment of collapse, should it occur, penicillin has proved itself invaluable.

Post-operative hæmorrhage is another condition which requires discussion, as this is one of the more common and sometimes disastrous complications which may occur. Allan and Welch<sup>1</sup> reported a mortality of 3 per cent. from post-operative hæmorrhage.

Slight post-operative hæmorrhage, which may be most distressing and cause nausea and sickness, and necessitate the use of suction, is most desirable.

In this series there have been 7 cases of slight hæmorrhage all of which settled with conservative treatment, but necessitated suction. There was only one serious post-operative hæmorrhage and his case is of some interest—a male, aged 40, who was admitted to a medical ward with a massive hæmorrhage, and was treated there for six days, during which time he required 11 pints of blood.

The hæmorrhage persisted and he was transferred to the surgical ward with Hb. of 35 per cent. Four more pints of blood were given rapidly and operation was carried out. There was a very large, indurated, fixed duodenal ulcer, and at the time it was considered too great a risk to attempt to remove it in view of the patient's poor condition. A partial gastrectomy was carried out but the ulcer was left *in situ*, the pylorus being closed after the method of Bancroft, and all the vessels in the region of the pylorus were ligated.

The following day, the patient's general condition was much improved and it appeared that the bleeding had stopped. This improvement was maintained for four days, after which there was a recurrence of massive bleeding which persisted for twelve days and necessitated the giving of a further 22 pints of blood, a total of 37 pints in all in three weeks, after which the bleeding ceased and the patient made a very satisfactory recovery and had no serious hæmolytic upset. Since this case I have determined never to shirk the exposure of the bleeding point if its site is obvious.

Unfortunately, this man is to-day a chronic alcoholic, but in spite of this, he has no dyspeptic symptoms.

Another complication which is commonly recorded in the literature as a cause of death—leakage from the duodenal stump—is included in the Table, but I have so far not encountered this and I feel that this is a strong argument in favour of the type of operation which has been described.

#### LATE COMPLICATIONS

(a) STOMAL ULCER.—I feel that the follow-up is not sufficiently long to assess the incidence of stomal ulceration, although it is generally supposed that these usually occur within the first two years, but I can see no reason to suppose that the incidence should be higher than in those cases who have a short loop posterior polya type of gastrectomy carried out.

There was, however, one case and he was instructive—a male, aged 59, with long-standing history—twenty years—of dyspepsia, and latterly pyloric obstruction and vomiting and a relatively low acid. The type of case, in fact, in which a gastro-jejunostomy might have been considered. In view of his age, the apparent low acid and poor general condition, a rather less radical gastrectomy was undertaken.

The immediate convalescence was uneventful, but four months later, he not only developed a jejunal ulcer, but also a gastro-jejuno-colic fistula, from which he ultimately succumbed.

This case illustrates my earlier point about the necessity for removing an adequate amount of stomach, at least two-thirds to three-quarters even in those long-standing cases who have a relatively low acid, as when the obstructive element is removed, the chronic gastritis which has reduced the acidity, improves, and hyperacidity recurs.

(b) DUMPING.—The dumping syndrome as defined by Custer, Butt and Waugh<sup>17</sup> of the Mayo Clinic, consists of four cardinal and almost invariable symptoms occurring fifteen to thirty minutes after food. They are :—

- (1) Profound nausea and weakness.
- (2) Generalised unpleasant feeling of warmth.
- (3) A cold sweat especially of the forehead and face.
- (4) Palpitation.

The cause of this syndrome is still debatable. There are three possibilities :—

(1) *Sudden Distension of the Jejunum*.—While sudden jejunal distension does cause a feeling of fullness immediately after food is swallowed and is exceedingly common after operations of the polya wide stoma type, it cannot be regarded as the primary cause of dumping, as when lævulose is used in place of dextrose to distend the jejunum, the flushing, sweating and lassitude do not appear.

(2) *Jejunitis*.—It has been observed that the majority of cases with the dumping syndrome show radiological evidence of jejunitis, but this may be in itself the result of too rapid emptying. In those cases in this series which have exhibited the syndrome, this has not been found to be the case.

(3) *Hypoglycæmia*.—It has been recognised for a considerable time that after gastrectomy or gastro-enterostomy, carbohydrates are more rapidly absorbed than usual.

This rapid absorption results in an over-stimulation of the production of insulin which in turn, leads to a sudden drop of blood sugar level and results in hypoglycæmia one to one and a half hours after food. Severe hypoglycæmia may induce the excessive secretion of adrenalin which may simulate in every respect the dumping syndrome.

Since, however, the dumping symptoms usually occur within half an hour after food, it will be seen that there is some room for doubt as to the validity of this theory. It may be, however, that the rate of fall in blood sugar level from hyper- to hypoglycæmia is associated with the upset.

The one constant feature which is present in all these theories is too rapid emptying of the stomach. As has been pointed out,

Gilbert and Dunlop<sup>14</sup> reported 35 per cent. of cases who had had gastrectomy of various types carried out presenting the dumping syndrome.

In this series there have been 17 cases (15 per cent.) from whom the dumping syndrome could be elicited by asking leading questions. Twelve of these were symptom free within three months of operation. Of the remaining five, three have only had a three months follow-up and are improving; one has persisted for two years; and one for one year. Both of these, however, are able to work. I think these figures compare very favourably with those to be found in Gilbert and Dunlop's series, where 10 per cent. were unfit for any form of employment because of the dumping syndrome.

It is interesting to note that a number of patients who presented themselves for operation had symptoms identical with the dumping syndrome pre-operatively. In all, except the five already referred to, they have completely cleared up after operation. It has been found by Abrahamson<sup>18</sup> that patients suffering from duodenal ulcer have a low blood sugar level. This is an interesting observation which we hope to investigate further.

It is probable that the small incidence of persistent dumping in this series is due to the delayed emptying time of the gastric remnant, due to the early development of a sphincteric-like action of the small stoma.

While many people believe that the size of the stoma has no influence on the emptying rate and that this is controlled only by the size of the lumen of the jejunum, this is not borne out by my experience. Forty cases have had follow-through barium series carried out, and the average time taken for the stomach to empty has been fifty-eight minutes. That is the time taken for the fluid level in the stomach to disappear. As opposed to fifteen to twenty minutes in cases who had had a full length anastomosis performed.

This delayed emptying is not due to any organic obstruction as during the first few days the stomach empties rapidly—barium flowing straight through into the jejunum immediately. The majority, however, have developed delay and sphincteric-like action within six weeks (Figs. 4, 5, 6 and 7).

In addition, I have recently had a case referred to me who had had a full-length polya type gastrectomy carried out eighteen months before, and who had such severe post-prandial dumping symptoms that it was necessary for her to lie down for one hour after every meal and who was afraid to eat in a public place for fear of fainting.

A second operation was performed reducing the size of the stoma to  $2\frac{1}{2}$  cms. Before operation the gastric remnant was completely empty in five minutes and there was marked jejunal bulging. After operation, emptying time was well over one hour and the patient was entirely symptom free within fourteen days and able to eat a normal full diet (Figs. 8 and 9, 10 and 11).



FIG. 3.—Barium meal carried out twenty hours after operation shows barium going straight into the jejunum.

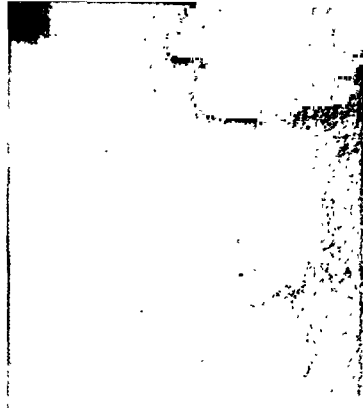


FIG. 4.—Immediately after barium swallow. Note size of stomach and barium entering jejunum.



FIG. 5.—Same case. Stoma closed and stomach dilated some minutes later.

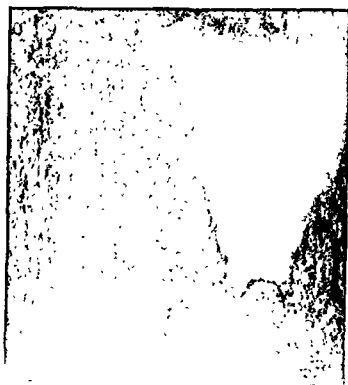


FIG. 6.—Same case. Stoma open and stomach contracting and passing meal on.



FIG. 7.—Same case. Stoma closed and only small amount of barium in first loop of jejunum.



FIG. 8.—Barium meal eighteen months after full-length stoma gastrectomy. X-ray immediately after swallowing barium. Note the jejunal bulge, the absence of a fluid level in the gastric remnant and the gross dilatation of the jejunum distal to the remnant.



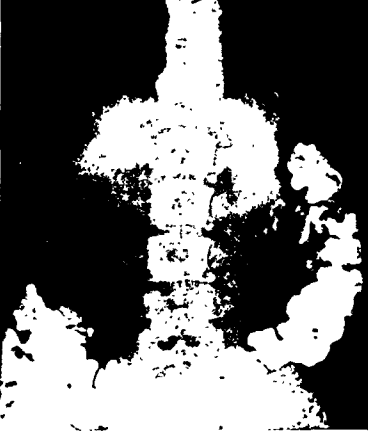


FIG. 9.—Follow-through X-ray one hour later shows the gastric remnant completely empty and all the barium is in the large bowel.



FIG. 10.—Barium meal of same case taken sixteen days post-operatively after stoma reduced in size to  $2\frac{1}{2}$  cms. X-ray fifteen minutes after barium meal. Note fluid level, absence of jejunal bulging and the delayed emptying. On screening the stoma was seen to have a sphincteric action.



FIG. 11.—Follow-through X-ray one hour later showing residue in the gastric remnant and stoma functioning.



FIG. 12.—Full length Polya type gastrectomy showing gross jejunal bulging and absence of true fluid level.

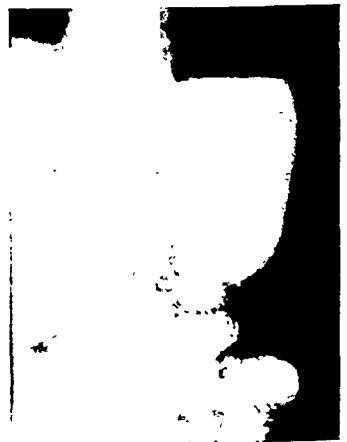


FIG. 13.—After small stoma type of gastrectomy—showing dilatation of gastric remnant and no overloading of jejunum.

## LATE RESULTS

It has been possible to follow up all the cases operated on ; all except two have reported personally. These two have been interviewed by their doctors, who have completed the questionnaire.

Since discharge three patients have died—one already referred to developed a gastro-jejuno-colic fistula : one developed an acute lobar pneumonia nine months later from which he died ; one—the case who developed post-operative small bowel obstruction—developed two attacks of acute obstructive jaundice four months later, and after exploration which revealed no stone the jaundice cleared up, but he developed a flare up of quiescent pulmonary tuberculosis which proved fatal. This man had had two perforations within six months before his gastrectomy, which was followed by re-operation for obstruction and four months later for obstructive jaundice, and I should hesitate to say that the flare up of tuberculosis was the direct result of the gastrectomy alone ; it was more likely due to the unfortunate sequence of operations over a very short period of one year. The remainder are all alive and well.

Except for one, who had been off work for sixteen years before operation with a stomal ulcer, and one who had been off work for fifteen years before operation, all of the remainder who have been followed up for more than three months have returned to their former employment : 84 per cent. of these returning in three months or under, and 24 per cent. in six weeks or under. In this 24 per cent. of cases there are included several who were able to undertake heavy manual work.

## DIET

Many people feel that gastrectomy is but one step in the treatment of peptic ulcer and that it is necessary for patients to continue on a strict ulcer regime after operation. This may be in part due to the fact that the majority of patients who have a large or full-length anastomosis carried out cannot eat a full meal. This has been shown by Vitkin<sup>19</sup> and others to be due to the fact that the gastric remnant remains small for a long period after operation—eighteen months or more—and that after eating there is gross jejunal bulging (Figs. 12 and 13).

One cannot help feeling that any major operative procedure directed at curing the patient must be regarded as a failure unless they can consume a full normal diet and lead a normal life.

In this series no case followed up radiologically showed gross jejunal bulging and all showed dilatation of the gastric remnant to three or four times its original size within six weeks of operation.

This has enabled 90 per cent. of cases to return to a full diet—normal in quantity and quality—within six weeks.

Ten cases were inadvertently directed to the Dietetic Out-Patient Department, but since their follow-up special diet has been stopped.

It is interesting that the only two cases who were anæmic occurred in this group.

It is obvious that the psychological effect of being able to eat anything and everything is very great.

Finally, the answer to the last question in the follow-up—"Would you advise a close relative to have this operation under similar circumstances?" was unanimously answered in the affirmative.

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## CAUSALGIA: A REVIEW OF 22 CASES

By A. J. SLESSOR, F.R.C.S.

(From the Department of Surgery, University of Edinburgh)

THIS review has been undertaken to ascertain the late results of sympathectomy for causalgia in a series of 28 patients out of 670 cases of peripheral nerve injury treated at a centre in India. The patients were all British and had been wounded in Burma; and the sole criterion on which a diagnosis was made was the presence of a spontaneous, severe, constant pain of burning quality, situated approximately in the sensory territory of a nerve which had been injured. The sites of injury, the nerves involved and the number of patients traced are shown in Figs. 1 and 2.

The review has, in some cases, been undertaken by personal examination and by questionnaire in others, since the patients are now widely dispersed. In addition, through the courtesy of colleagues in other hospitals, it has been possible to see the records of 14 patients who have received treatment in this country.

### CLINICAL FEATURES

*Subsidiary Pain.*—The frequency with which pains of a different type accompanied burning pain was of note (Table I) and has been recorded by other observers (Kirklin *et al.*, 1947). A number had

TABLE I

*The Incidence of Subsidiary Pain Associated with Burning, 22 Cases*

Complaint.	Upper Limb. 13 Cases.	Lower Limb. 9 Cases.	Total.
Crushing . .	6	3	9
Bursting . .	6	2	8
Clenching . .	5	2	7

more than one subsidiary pain; none had all three. Subsidiary pains were described as (1) crushing, as if the hand or foot were locked in a vice, or squeezed between two blocks of wood—the latter a common description; (2) bursting, as if a balloon were being blown up within the hand or foot, and (3) clenching, as if the fingers or toes were being bent forcibly towards the palm or sole, a symptom often associated with the presence of a painful phantom limb in the upper extremity.

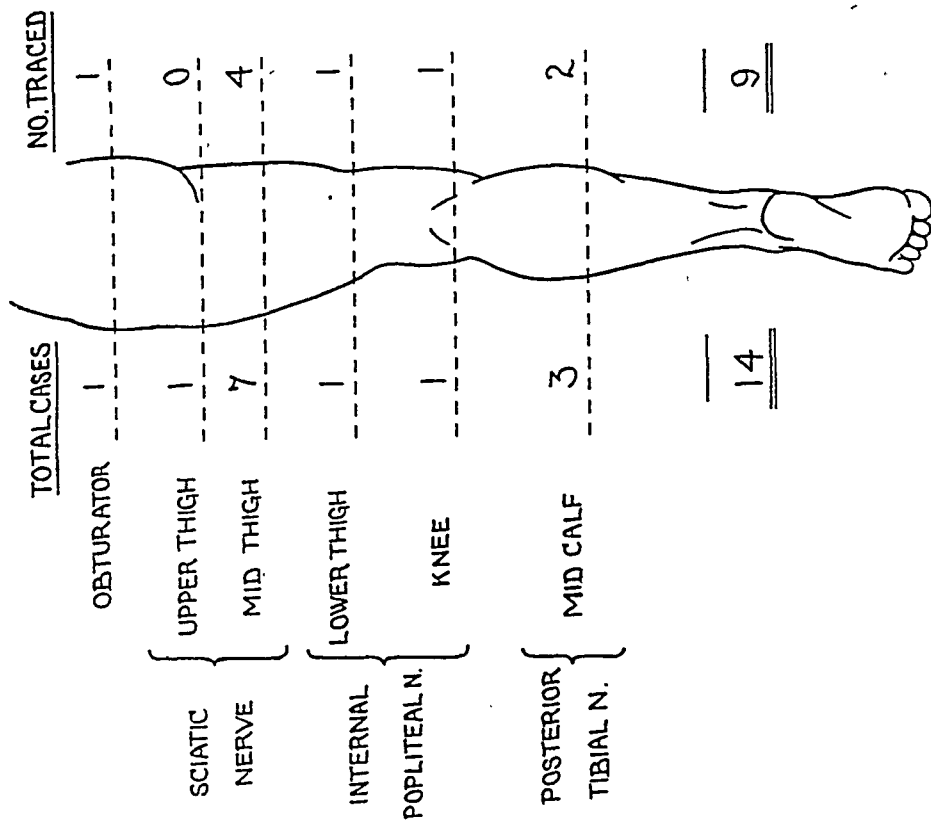
CAUSALGIA - LOWER LIMB

FIG. 2.

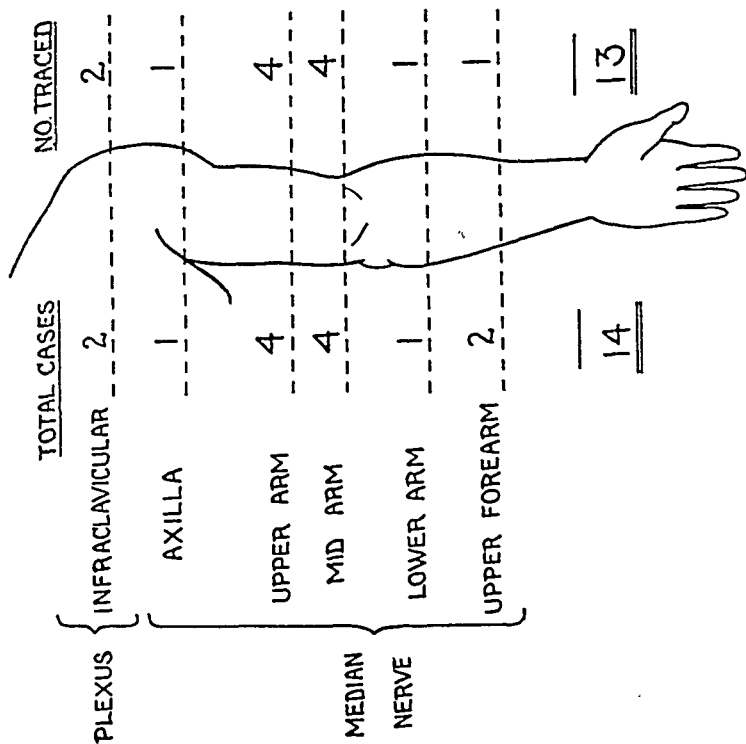
CAUSALGIA - UPPER LIMB

FIG. 1.

Stabbing, knife-like pains are too commonly present in partial peripheral nerve injuries uncomplicated by causalgia to be regarded as part of the syndrome of causalgia.

*Response to Emotional Stimuli.*—The response to emotional stimuli corresponded closely to that observed by others (Goodman *et al.*, 1946; Allbritten and Maltby, 1946; Kirklin *et al.*, 1947). As emotional stimuli are included such examples as the approach of a surgeon, the sight of someone tripping (or even the expectation that he might trip), sudden noises, whistling, the passage of aeroplanes overhead, and the thought of heights and high buildings. Fifteen of the 22 patients stated that emotional stimuli seriously aggravated the burning feeling, and also any subsidiary pains; in six moderately severe aggravation occurred, and one was apparently immune to this form of stimulation although his was amongst the severest of the causalgias.

*Response to Environment.*—In India, the effect of heat was most pronounced. In the hot season, these men, miserable enough already, became doubly so during the hottest part of the day, when the shade temperature was perhaps 110° F. They would not in any circumstances expose the affected limb to the direct rays of the sun, and those with injuries of the upper extremity would run the 20 yards to the lavatory in another building. Only one patient, who differed from the others in no other respect, did not suffer exacerbation of pain during the extreme heat. It was found that coolness in some form afforded relief, whether it was the relative coolness of the night (when the temperature might still be 90° F.) or that obtained from the application of a cool, wet cloth around the affected part; it was so apparent that the coldest water available was always used that I felt sure it was the coolness, rather than the wetness, which was the relieving factor in so-called hygromania. Three patients did not obtain relief from cool water, and one found it an aggravating factor; in all other respects, these three were typical cases.

*Vasomotor Phenomena.*—All affected limbs were warm, and indeed no other findings could be expected in any case of peripheral nerve injury in such environmental temperatures as have been mentioned.

*Hyperaesthesia and Hyperhidrosis.*—These were present together in 15 cases; in no case was either found alone. They are not necessary features of causalgia (Spiegel and Milowsky, 1945), and are present in many patients with partial nerve injuries, irrespective of spontaneous pain. When first seen, two patients had on clinical examination a total nerve lesion. One of them had an infraclavicular brachial plexus lesion, but the burning pain was restricted to a large median territory; the other patient had a median nerve causalgia, with total motor and sensory loss. That causalgia may occur with a lesion which is complete on clinical examination has been observed elsewhere (Kirklin *et al.*, 1947).

*The Association of Vascular Injury.*—Injury to main vessels

occurred in six of the 22 cases (Table II). There would appear to be no definite relationship between causalgia, and the association of vascular with nerve injury (Spiegel and Milowsky, 1945).

TABLE II  
*Association of Major Vascular Injury*

Site.	Nerve Injury.	Vascular Injury.
Upper limb . . .	Brachial plexus (2 cases) Median nerve (11 cases)	1 (axillary artery ligated) 4 (1 axillary vein ligated; 3 brachial artery spasm)
Lower limb . . .	Sciatic and divisions (8 cases) Obturator (1 case)	1 (popliteal artery ligated) ... - 6 -

*Relationship Between Onset of Pain and Severity of Causalgia.*—In the majority of my patients, the burning pain was felt within an hour of the receipt of the wound; the latest onset (five days after wounding) was in a patient with a partial lesion of the sciatic nerve. It could not be established that there was any difference in intensity of pain between those with a delayed onset and those whose causalgia was felt immediately.

*Psychological Aspect.*—There was no evidence that at the time of wounding there was in any patient any inherent psychological abnormality which predisposed to the development of causalgia. It is true that some patients were more upset than others; all had been in combat, and no doubt they reacted differently in action just as they reacted differently to pain. After successful treatment, instead of being moody and introspective, these men became normal and enjoyed life as much as their fellows. Mayfield and Devine (1945) submitted 15 cases to psychiatric analysis, and each patient was classified as a normal individual with a stable personality.

### TREATMENT

The treatment employed in the 22 traced cases is shown in Table III. It is of interest that, although three patients with lower limb injuries were regarded as having causalgia of intensity so low that no special

TABLE III  
*Treatment in 22 Cases*

Treatment.	Upper Limb.		Lower Limb.		Total.
	Brachial Plexus.	Median Nerve.	Sciatic and Divisions.	Obturator.	
Sympathectomy by operation . . .	2	9	6	0	17
By repeated sympathetic novocain block	0	2	0	0	2
No special treatment . . .	0	0	2	1	3

treatment was necessary, all the cases of causalgia in the upper limb were thought to require treatment. My impression is that causalgia of the upper limb tends to be more severe and more susceptible to emotional and environmental aggravation than that occurring in the lower extremity, an impression confirmed by other observers (Kirklin *et al.*, 1947).

When a definite diagnosis had been made, the routine treatment adopted was to block the sympathetic chain to the affected limb by paravertebral injection of 1 per cent. novocain; for the upper limb the needle was inserted below the 2nd rib and transverse process, and for the lower limb above the 2nd, 3rd and 4th lumbar transverse processes. In all cases relief was obtained, which lasted usually for one and a half hours, and occasionally longer. Two patients noted a lasting reduction in severity of pain following paravertebral injection; they were re-injected three and four times respectively at intervals of three days, each injection producing further relief until they were free from pain and regarded as cured. In the majority, whose pain returned to its former intensity as the effect of the novocain wore off, operation was performed if the pain was considered severe enough, the decision being made mainly by the patient, after he had experienced the temporary relief from injection; and as has been indicated, only three of the 22, and the two cured by repeated paravertebral injection, were held to be outwith this category.

In the upper limb, the denervation was achieved by section of the thoracic chain below the 3rd ganglion, with separation of the 2nd and 3rd ganglia from all rami; in six, in addition the 2nd and 3rd intercostal nerves were resected, as recommended by Smithwick. In the lower limb, the 2nd and 3rd lumbar ganglia were extirpated through a muscle-cutting lumbar retroperitoneal approach; at the time I was not aware of the view that in cases of high sciatic injury, it might be necessary to remove the 1st lumbar and even the lowest thoracic ganglia (Mayfield and Devine, 1945), but it happened that all the treated sciatic lesions were at mid-thigh level or lower.

*Results.*—All 17 patients treated by open operation were relieved; in only one was pain not completely abolished, and he estimated the improvement at 75 per cent.; two returned to active combatant service.

The success of repeated novocain injection in two cases has already been referred to.

#### PRESENT CONDITION

*Patients Treated by Operation.*—At the time of writing, all the patients in this series are working, and the occupations of those who suffered from causalgia of the upper limb include dance-band drummer, bus conductor, signwriter and non-commissioned officer in the Royal Marines; while among the lower limb cases there is a lumberjack in Finland (a training self-imposed by a forestry student), a farmer who hunts and a general labourer.



The two patients described as having complete lesions have shown spontaneous nerve recovery; the patient with the infraclavicular brachial plexus injury is working as a decorator and painter, and the patient with the complete median lesion is a bench hand, although associated radial and ulnar palsies have reduced the function of his hand appreciably. The present symptoms of this group may be compared with those before operation (Table IV). It will be seen that all have remained free from burning pain for two to three years.

TABLE IV

*Present Symptoms Compared with Pre-operative Symptoms  
Two to Three Years Ago*

Complaint.	Upper Limb.		Lower Limb.	
	Pre-operative.	Now.	Pre-operative.	Now.
Burning . . .	11	0	6	0
Crushing . . .	5	2 Slight	3	2 Slight
Bursting . . .	5	1 Slight	2	0
Clenching . . .	3	1 Slight	2	1

Some have a mild degree of subsidiary pains. Of the 17 patients, three show clinical evidence of incomplete sympathetic denervation, either as a result of faulty operative technique or of regeneration; but they also have remained free from burning pain, nor have they an undue share of subsidiary pains.

Emotional stimuli, so-called, continue to have some effect on six patients, of whom only one is known to be incompletely sympathetomised. When excited, these six experience what they describe as an unpleasant feeling in the limb, but there is no burning, and the sensation is felt throughout the limb, in contrast to the relatively small pre-operative causalgic area. The patient who is working in Finland finds, even now, that the thought of high buildings, or seeing them, will cause this vague unpleasantness in the affected leg.

In cold weather, the affected limbs tend to become stiffer, colder, and slightly more cyanotic than normally, especially the upper extremities. The feet of those with sciatic injuries, if suitably clad, do not have the same tendency to enter this cold phase. This difference in the behaviour of the upper and lower limbs corresponds to that found in peripheral nerve injuries uncomplicated by causalgia (Richards, 1946), and it is of note that the student in Finland did not find that 60° F. of frost affected the wounded limb more than the normal one, if both were equally protected. In no instance did cold cause a recurrence of burning pain. The effect of heat is less easily estimated in this island; yet even here summer may aggravate

untreated causalgia, as is indicated by two patients (not included in this series) who had had causalgia for three and six years respectively, and who "dreaded the onset of summer." \*

In general, it may be said that the response to heat has simulated that found in nerve injuries uncomplicated by causalgia, in that the affected limb becomes warmer, more mobile and functionally more useful; there has been no recurrence of burning pain in any patient. This applies equally to those known to be incompletely sympathectomised; one of the three is in Barbados, and he does not find heat an aggravating factor although his leg sweats in the territory of the long saphenous nerve. The response to heat and cold appears to resemble that of an old uncomplicated peripheral nerve injury rather than that obtained by preganglionic sympathectomy. This suggests that the original local nerve lesion must have interrupted at least a very considerable proportion of the sympathetic efferents within the nerve.

All 15 patients who were noted to have hyperæsthesia and hyperhidrosis before operation were relieved of both after operation. A number of those with upper limb injuries find that stimulation of the sensory territory of the affected nerve causes mild paræsthesiæ in its distribution, invariably described as pins and needles or tingling. Such a response is common in partially recovered nerves irrespective of causalgia, whether the recovery is spontaneous or follows suture, and in the patients under review was no doubt present before operation, but masked by the spontaneous burning and by the extreme sensitivity to local stimulation. Hyperhidrosis was of course abolished by sympathectomy.

*Patients Treated by Repeated Injection.*—Of these two patients with causalgia of median distribution, one, who returned to full active service initially, is now working as a market gardener, with a pain-free limb which, he says, is "very nearly normal, only it is slightly wasted." The other is a poultry farmer, pain-free, but with the function of the hand impaired by inability to use the thumb and index finger.

*Patients who had no Special Treatment.*—Of the three untreated cases, whose causalgia was not regarded as sufficiently severe to require sympathetic interruption, two had sciatic nerve injuries and one an obturator nerve lesion, with burning and hyperæsthesia following a wound in the groin (Fig. 3). These men still have causalgia, although its intensity is diminishing very slowly. They respond briskly to emotional stimuli; the patient with obturator causalgia mentions "train whistles, motor horns, seeing someone trip or fall" as causes of aggravation of the burning. Heat, for example proximity to a fire, increases the pain, coolness relieves and cold tends to aggravate it. They are all working, but one wonders whether they might not be happier men had sympathectomy been performed three years ago.

\* Recently performed sympathectomies on these patients have afforded considerable relief, complete in one patient, even after these intervals.

It is of note that one, on whom a neurolysis was performed, received no benefit from the operation; the nerve was explored, not in the hope of relieving the causalgia, but because of total external popliteal nerve palsy in association with a partial internal popliteal nerve lesion; it was thought that the external popliteal nerve might be divided. At operation both nerves showed slight intraneural scarring and thickening, with surrounding soft tissue fibrosis; the lesion of the internal popliteal nerve was typical of any partial nerve injury and there was nothing to suggest why it had occasioned causalgia.

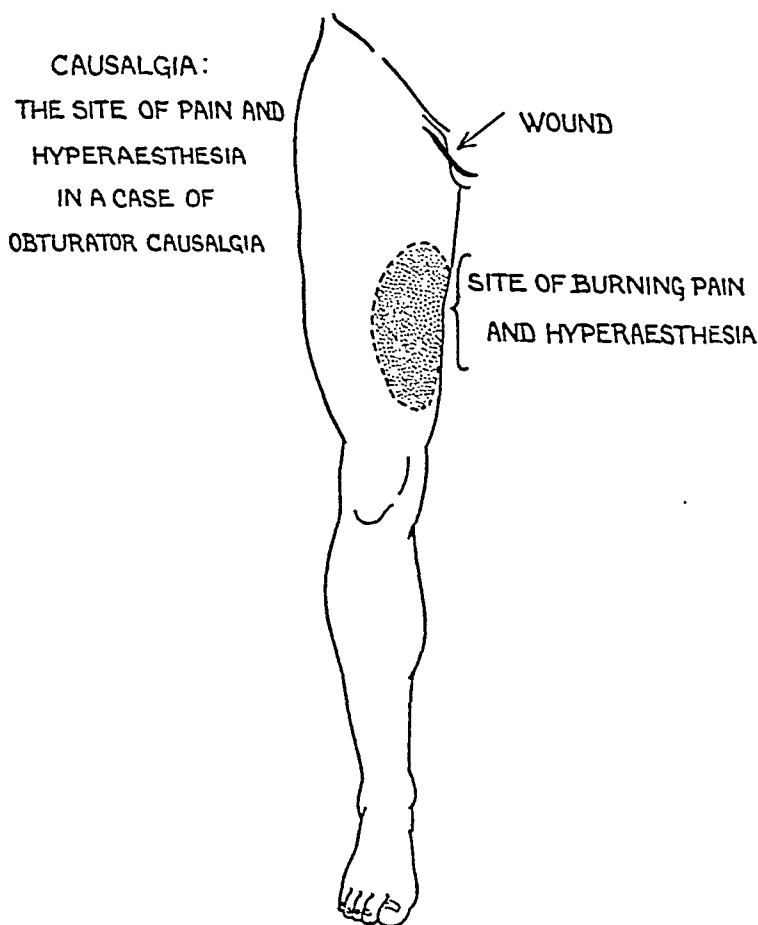


FIG. 3.

### CONCLUSIONS

(1) Sympathectomy relieves the burning pain of causalgia; in 17 patients so treated there has been no recurrence of this pain two to three years after operation. Subsidiary pains may persist, although diminished in intensity.

(2) In a proportion of cases, repeated novocain block of the appropriate sympathetic chain affords relief; two patients so treated have remained pain-free for three years.

(3) Slight sympathetic activity in the limbs, the result of faulty operative technique or of regeneration, has not been associated with recurrence of symptoms.

(4) Three untreated cases still have causalgia, which is gradually diminishing, although emotional and environmental stimuli continue to aggravate the pain.

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## NEW BOOKS

*The 1946 Year Book of Obstetrics and Gynecology.* Edited by J. P. GREENHILL. Chicago: Year Book Publishers, Inc. Price 21s.

There are at least five journals which publish extensive abstracts of obstetrical and gynaecological literature. These, together with the Year Book, ensure that the busy obstetrician cannot plead that he has not sufficient time to read his journals. Here is global literature boiled down to a minimal pabulum!

Professor Greenhill has a unique and honoured place as a critic, and his annual *Year Book of Obstetrics and Gynecology* is welcomed by those of us who appreciate his excellent summaries and particularly his editorial comments which follow the pungent style of the late Joseph De Lee. The literature of 1946 is adequately covered and, moreover, ample space is devoted to publications from outside America.

*Utero-tubal Insufflation.* By I. C. RUBIN, M.D., F.A.C.S. Pp. 453, with 159 illustrations and 900 references. London: Henry Kimpton. 1947. Price 50s. net.

It is generally agreed that dysfunction and pathology of the Fallopian tubes account for some 30 per cent. of cases of female sterility. This fact prompted Professor Rubin to make a special study of the subject and now, following many authoritative contributions to the literature, comes this book which provides us with the fruits of over thirty years of progressive and accumulated knowledge. Radio-opaque substances were utilised for the purpose of outlining the Fallopian tubes from 1914 but it was in 1919 that Professor Rubin conceived the idea of testing the patency of the tubes by insufflation with air. Since then he has gradually perfected the technique of gas insufflation and has shown how study of kymographic records will reveal a wide variety of both normal and abnormal changes in the tubes. Much of the book is concerned with the interpretation of graphs and this aspect of the investigation is of the utmost importance if full use is to be made of the Rubin test. Of particular interest are the chapters devoted to the evaluation of insufflation and hystero-salpingography in relation to diagnosis, therapy and the incidence of complications and sequelæ. In the experienced hands of the author the former procedure gives the greater amount of information and the lesser upset. Whereas the wealth of detail in anatomy, physiology, pathology and technique make this book indispensable to those actually concerned in the investigation of female sterility, its appeal will embrace all those with an interest in this ever-present problem of domestic, national and world-wide importance.

*Obstetrics and Gynecology.* By C. SCOTT RUSSELL. Pp. viii+214, with 21 illustrations. London: Geoffrey Cumberlege. Oxford University Press. 1947. Price 12s. 6d.

This small book has been written to help ex-Service doctors returning to civilian practice to pick up the threads of practical obstetrics and gynaecology. References are provided throughout the text so that, where interest has been stimulated, a full study can the more easily be initiated.

Easy to read, it outlines the main points in the diagnosis of the commoner conditions, indicates the scope of the newer methods of investigation, such as radiological pelvimetry, and discusses briefly, treatment. Attention is drawn to recent advances in therapeutic measures and to modern conceptions of obstetrical management. One of the most important factors in the latter, the reader will sense, is the need for close co-operation and team work between the general practitioner and the maternity hospitals.

*Radical Surgery in Advanced Abdominal Cancer.* By ALEXANDER BRUNSCHWIG. Pp. 324, with 117 illustrations. The Cambridge University Press. 1947. Price 42s. net.

The author of this book is Professor of Surgery in the University of Chicago. The work is a careful record of one hundred cases of advanced abdominal cancer in which treatment by surgical operation was undertaken; most of the cases would be regarded by the majority of surgeons as inoperable. The scope of the operations undertaken in many of the cases is truly heroic; the most extensive consisted of total gastrectomy-splenectomy-resection of body of pancreas, transverse colon, portion of left lobe of liver, fascia and musculature of left upper quadrant of abdominal wall and upper retro-peritoneal tissues, but on the same page are mentioned two cases in which total gastrectomy, splenectomy, and resection of the body of the pancreas were carried out, with removal of the transverse colon in addition in one case. The operative mortality was 34 per cent. Nineteen per cent. have survived for one and a half years or longer, one for ten years, one for nine, two for five and a number for four years. In 30 per cent. there was appreciable palliation with survival to one and a half years or a little longer, while in 17 per cent. there was no palliation. It would be easy to suggest that operations of the severity described are unjustifiable, but the results achieved in an otherwise hopeless disease prove that this is not the case. The determination and technical skill employed in these extensive operations command our whole-hearted admiration. As a result of the experience gained in these cases the author concludes, that the only limits to operative resection of intra-abdominal structures are the limitations afforded by the minimal requirements of certain structures for normal physiological activity. The book contains a most valuable chapter on the "supportive" measures which have enabled the patients to withstand such severe ordeals.

*Malaria with Special Reference to the African Forms.* By W. K. BLACKIE, M.D., PH.D., F.R.C.P.(ED.), D.T.M. AND H., with Foreword by Professor F. FORMAN, M.D., F.R.C.P. Pp. viii+104, with one colour plate. Capetown: For the Post-Graduate Press by the African Bookman. Price 10s. 6d.

Acute malignant malaria makes African and European children kin, "A child taken ill in the morning may be dead by evening." The rest of the story of malaria as it affects African and European is clearly told in this "essentially clinical monograph," the more readable, for the history in it, for a willingness to repeat in season, and for a scarcity of textual slips. Interim answers are given to questions of the dosage and efficacy of Paludrine.

More about malaria from this source will be awaited with interest, and perhaps enough about blackwater fever to earn it a place in the index next time.

*Studies of the Renal Circulation.* By J. TRUETA, M.D., D.SC., A. E. BARCLAY, O.B.E., D.M., F.P.C.P., D. M. DANIEL, M.A., M.B., K. J. FRANKLIN, D.M., F.R.C.P. and M. L. M. PRICHARD, M.A. Pp. xix+187, with 83 illustrations. Oxford: Blackwell Scientific Publications. 1947. Price 25s. net.

This work describes the results of several years research carried out in the Nuffield Institute at Oxford. It is an excellent example of the value of team work produced by the collaboration of physiologist, pathologist, radiologist and clinician.

The authors report a discovery of fundamental importance. They have found that the circulation in the kidney does not constantly follow a definite pattern. The vessels of the organ may be divided into two separate fields so that at one time most of the blood is diverted to the cortex, at another to the medulla or again through both pathways though in varying amount. They discuss some of the clinical and pathological implications of their findings which may be of practical importance.

The book has been well produced on high class paper and shows little evidence of war-time restrictions. It is a monograph of first-class importance.

## BOOKS RECEIVED

- BARNES, JOSEPHINE, M.A., D.M.(OXFORD), M.R.C.P.(LONDON), F.R.C.S.(ENG.), M.R.C.O.G. Gynæcological Histology. (*Harvey & Blythe Ltd. London*) 30s. net.
- BAILEY, HAMILTON, F.R.C.S.(ENG.), F.A.C.S., F.I.C.S., F.R.S.E., and LOVE, R. J. MCNEILL, M.S.(LOND.), F.R.C.S.(ENG.), F.A.C.S., F.I.C.S. A Short Practice of Surgery. Part Two. Eighth Edition in 5 Parts. (*H. K. Lewis & Co. Ltd., London*) £2, 12s. 6d. the set.
- CARRUTHERS, DOUGLAS G., M.B., CH.M.(SYDNEY), F.R.A.C.S. Diseases of the Ear, Nose, and Throat. Second Edition. (*John Wright & Sons Ltd., Bristol*) 25s.
- COMFORT, ALEX., M.A., M.B.(CANTAB.), D.C.H. First-Year Physiological Technique. (*Staples Press Ltd., London*) 7s. 6d.
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- Edited by DELLER, F. CROXON, M.D., M.R.C.P. The Modern Management of Gastric and Duodenal Ulcer. (*E. & S. Livingstone Ltd., Edinburgh*) 20s. net.
- Edited by PARKER, FRANCIS P., M.D. A Textbook of Clinical Pathology. Third Edition. (*Bailliere Tindall & Cox, London*) 50s. net.
- FROHMAN, BERTRAND S., M.D. Brief Psychotherapy. (*Henry Kimpton, London*) 20s. net.
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# Edinburgh Medical Journal

October 1948

## THE MEDICAL MAN IN THE WITNESS BOX

By SHERIFF T. B. SIMPSON, K.C.

ALTHOUGH the officials of the Medico-Chirurgical Society had no possible means of knowing it when they arranged this meeting, to-day is an anniversary of considerable importance in my life. Thirty-nine years ago to-day Mr H. J. Stiles, in an emergency operation, removed my appendix, thereby giving me a life-span far beyond anything which I could reasonably have expected, having regard to the previous medical history both of my family and of myself. Mr Stiles and I were both gainers; I got thirty-nine years plus; he got a fee which measured in terms of to-day's spending power and taxation represented roughly one year's salary under the National Health Act *and* an appendix of roughly (I gather) the size and shape of a banana, about which he lectured to the day of his retirement. After the operation I had a tube in my side for purposes of drainage, and lying on a bed the head end of which was raised above the floor on wooden blocks, I was three or four times knocked off these blocks during the first week, and from that experience no doubt dates that whole-hearted devotion to the medical and nursing professions which alas! I have had only too ample opportunities of displaying during all the subsequent years. About ten years ago I gave the Harveian Society the full catalogue of my medical and surgical past; indeed at their special request my heart is to be made available to them for their first annual dinner occurring after my decease; and I have no intention of repeating that long and melancholy list now. I only say that to that list there falls to be added an illness three years ago which, after keeping me in bed for five months has since kept me out of active practice at the Bar. Looking to these facts, I feel that I am in a peculiarly strong, cross-bench sort of position to open a discussion of the kind we are to have to-night.

In starting to consider what was to be said about the relationship of the court lawyer to the doctor I was reminded of the opening of the new Law Courts in London in the 1870's. The Queen was to attend the opening in person and Her Majesty's judges were to present her with a loyal address. They assembled to consider its terms and a draft was read which contained the expression, "conscious as we are of our imperfections." Some of those present objected to the phrase as being unduly humble and self-depreciatory (judges had a

Paper given to Medico-Chirurgical Society, 2nd June 1948.



robust self-confidence in those spacious days wholly lacking in their successors), and Lord Justice Bowen, who was present, said that their objections might be met, and the truth adequately presented, by a trifling amendment. Let the phrase be altered to "conscious as we are of one another's imperfections." That phrase floated, unbidden, into my mind as representing the mutual relation of doctor and lawyer. Is it true? It has never been my own attitude. I certainly entertain no strong feeling that doctors are not good witnesses, nor can I work up any sense of professional indignation against them in the witness box, or even out of it. Indeed my first reaction on hearing the subject of to-night's discussion was to think that "doctors are no worse in the witness box than any other kind of witnesses," and my own debt to doctors is far too great for me to be able to generalise against them.

Still, the implications of that Bowen story remain, and I suppose that generally speaking it is true to say that doctors look on lawyers as hide-bound pedants, with a snuffy adherence to old-fashioned rules, people who before they come to any conclusion have to ask themselves "what did Lord Mansfield say in 1779?" To which the poor lawyer can only reply that while what Lord Mansfield said in 1779 may still be *true*, the only *certainly* about medicine is that in fifty or a hundred years the doctors will be casting just as much ridicule on *everything* done by the practitioners of to-day as we do on the prescribers of snails' broth and puppies' urine, with as much justice and for much the same reasons.

So, I do not propose to look on this meeting as a debate, in which I am to sustain the thesis that all doctors are fools, while Dr Slater is to reply in an angry philippic designed to show that all lawyers are knaves. My task is really to start some topics for discussion, and I have been instructed to keep the discussion on lines as broad as possible. This suits me, since like the Declaration of Independence I have a weakness for the "glittering generality." What I propose to do is to mention one or two cases where my own practice has impinged on medicine, and to touch on some of the lessons which may be derived from them. Being no longer in practice I cannot be suspected of self-advertisement, and I think it is perhaps a more interesting line of approach than an attempt to construct *a priori* a theoretical conspectus of the subject, with reference to (or largely extracted from) the textbooks. Incidentally, when looking in the legal medical textbooks I was interested to discover one which was almost entirely devoted to the subject of our discussion to-night. Called *Law and Medical Men*, it was published in Canada in 1884. You will perhaps be disposed to think that it is unworthy of serious consideration by a Society such as this when I tell you that the subject of chapter I was, not the Hippocratic oath, not a Doctor's Duty, but "Fees," and chapter II "Who Should Pay the Doctor?" Chapter III went on, naturally enough, to "Negligence and Malpractice," followed in chapter IV by "Criminal Malpractice." Subsequent chapters in

this remarkable book dealt with "Defamation" and (oddly enough) "Dissection and Resurrection."

I begin with what is generally supposed to be the great battleground between the medical and legal professions, viz. the question of criminal responsibility in those who are suffering from one form or another of mental abnormality. "Would he have done it if a policeman had been watching him?" asks the lawyer; "If not, drag him to the scaffold." "Did he have bad dreams when he was a child?" asks the doctor; "Or, even worse, did his grandmother have bad dreams when she was one? If so, give him a rest cure in the Broadmoor Nursing Home." These are the extremes, and in between some working rules have been devised, under which rough justice has upon the whole been done. What is called the rule in *McNaghten's case* has been incorporated in the law of Scotland, but it has been followed in a commonsense sort of way, with a lack of the rigidity into which rules seem so readily to harden south of the Tweed. Modern refinements do not seem, to me at least, to have improved our law in this regard and there is a real danger (perhaps some of you do not consider it a danger) that all crimes of violence should go altogether unpunished. For an example of such refinement one of our more eminent modern judges, shortly before going on the bench, spatch-cocked into our law that a man charged with killing another on the road is entitled to a verdict of not guilty if he can establish that "by the incidence of temporary mental dissociation due to toxic exhaustive factors he was unaware of the presence of the deceased on the highway and of his injuries and death, and was incapable of appreciating his immediately previous and subsequent actions." Looking at the report I note that the toxic exhaustive factors in that case included food, tea, whisky and soda, sherry, coffee and "a young lady with whom [the accused] was on terms of friendship." It is true that the same judge, when confronted on the bench with this little piece of nonsense, would leap three feet in the air and detonate in every direction; but his legacy remained.

Where law and medicine, acting in concert, seem to me to have gone furthest wrong in this respect is in the manufacture of an intermediate class of abnormal criminal who is presumed capable of forming the intent to commit culpable homicide but incapable, by reason of his criminal abnormality, of forming the intent to commit murder! Incidentally, I wonder if this distinction would ever have come into existence at all if we had not had a death penalty for murder. "Our law [always under pressure, be it observed, by the medical specialists] has come to recognise *in murder cases* [a class of] those who, while they may not merit the description of being insane, are nevertheless in such a condition as to reduce the quality of their act from murder to culpable homicide." (L. J.-C. Alness in *H.M. Adv. v. Savage* 1923 J.C. 49.) That this provision has worked its way into our law is undoubted. Its illogicality is so obvious that over and over again the judges have emphasised that the rule "must be applied

with care." Especially do they emphasise that, in order to have the benefit of the rule a man must suffer from actual or "objective" weakness of intellect, aberration of mind, mental unsoundness, partial insanity, great peculiarity of mind, and the like. (L. J.-C. Cooper in *H.M. Adv. v. Braithwaite* 1945 J.C. 55.) The warning was sounded a generation ago by Lord Johnston, but his words have been disregarded, and I daresay that some mental specialists at least will say that his rule was narrow-minded and wrong. What he said, in rejecting the rule which is now part of our criminal law, was *inter alia* this: "To say that that man is mentally capable of murder and this man only mentally capable of culpable homicide, that that man is capable of a capital offence, but this one only of an offence not capital, is a proposition which would, I think, unsettle the administration of criminal law. [That, under the lead of the psychologists, is just what it is doing.] I can understand limited liability in the case of civil obligation, but I cannot understand limited responsibility for a criminal act. I can understand irresponsibility, but I cannot understand limited responsibility—responsibility which is yet an inferior grade of responsibility." (*H.M. Adv. v. Higgins* 1914 J.C. 1.)

Let me give you a concrete illustration, from my own experience, of the way in which this rule works and then leave it to those more expert than I am to suggest what the remedy should be. In 1944, acting in accordance with the practice whereby any person charged with murder in Scotland is provided gratis with the services of a King's Counsel, I went through to Glasgow to defend a man so charged. To defend a person on a capital offence is always a heavy responsibility (I have known only one counsel who *liked* taking such cases and needless to say he didn't do them very well), but in this case I had the comfort of knowing that the facts were really indisputable and that no one could put the noose more firmly about my client's neck than he had already done himself. He was a married man who had conceived an infatuation for a young, unmarried woman. He met her one afternoon, by arrangement, in a railway goods station about which his duties took him, and they were seen laughing and talking on the platform. A few minutes later, they were found in a van, with the girl lying strangled on the floor. The accused made no bones about having strangled her. Indeed, his first words were "I have done her in." A special defence of insanity had been lodged. Its slender foundations were that anyone who chose to commit murder in a station swarming with detectives, as this one was, and as he knew, "must have been mad"; also it appeared that the accused was unduly sensitive to ridicule, and that the girl had been laughing at him. Several doctors were prepared to state for the defence that a man who lost his temper on such an occasion to the extent of "seeing red" was in fact insane. (The logical result of that of course would be that no one could ever be tried for a crime of violence.) But it proved unnecessary to call them, since to my satisfaction the Crown doctors

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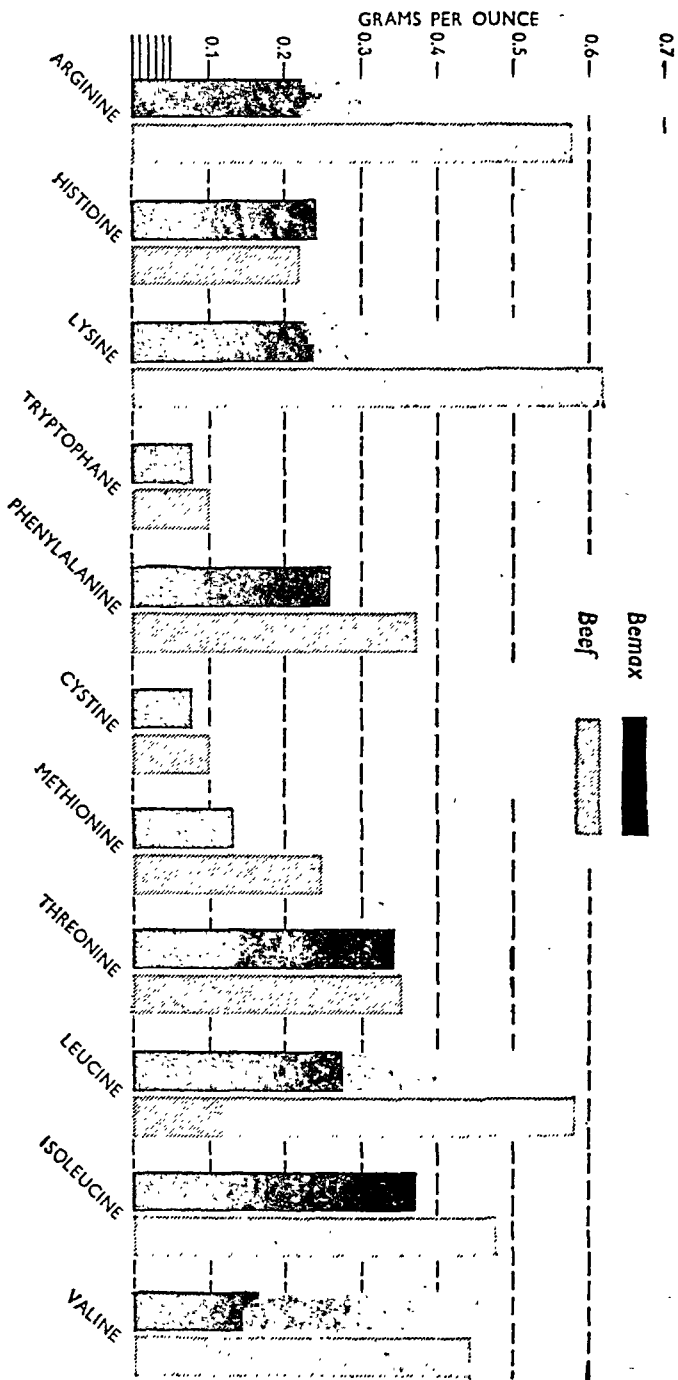
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admitted to me that the man "must have been mad," except for the stout-hearted Dr Ivy Mackenzie who said, in spite of all that I could do to persuade him otherwise, that the accused was as sane as a man could be. My satisfaction was not shared by the judge, who was none other than the inventor of "toxic exhaustive factors," and was palpably eager to hang my client. At the end of the Crown's case, the Advocate-Depute offered to accept a plea of culpable homicide under the rule I have been discussing. I asked for an adjournment to interview the accused, and plainly stated to him the alternatives. We could either run the case to an end, in which case he would undergo the risk, not a very great one I thought, of a capital sentence; or his defence of insanity would succeed, in which case he would be detained for an indefinite period in Perth Criminal Lunatic Asylum; or we could close with the Depute's offer, and he would get a very substantial sentence of penal servitude—I mentioned twenty years. He chose the last without hesitation, and amused me by commenting on the second alternative "would they send me to an asylum? it would be enough to drive me potty." He was lucky enough to get away with ten years penal servitude. I only remark in parting from him, as I now do, that, although he was unable to provide any fee for his poor counsel, he had been able to wash down his mid-day meal, on the day of what I must call, I suppose, the "culpable homicide," with two pints of beer and two glasses of whisky. But is that a satisfactory rule, and if not what should be done about it?

Another murder case in which I was engaged, now a good many years ago, was concerned with a number of medical questions, and may suggest some useful reflections on the medical man in the witness box. Judges have, or used to have, a habit, perhaps more prevalent in England than here, of referring to crimes of which they disapprove as "un-British." On this, "what *is* a British crime?" an enquirer asked of an experienced English judge, who without hesitation answered "kicking one's wife to death." That, more or less, was the subject of a murder trial in Inverness when I assisted the Crown to prosecute what in a contemporary record I described as "an amiable looking elderly gentleman [he was fifty-five] with a white moustache and gold-rimmed glasses, like a respectable edition of . . ." [here I gave the name of a then well-known advocate], who was charged with the murder of his wife. Post-mortem examination disclosed that besides having a black eye, bruises on her forehead, and a wound in her neck the deceased woman had apparently been kicked all over. She had thirty injuries. I now quote again from my record: "The defence put forward was that the woman died, not of bruises, etc., but of an obscure disease called Pachymeningitis hæmorrhagica interna. One of the hired assassins from Aberdeen, asked by the judge to explain this disease "in popular terms," replied: 'In popular terms I should say it meant simply a hæmorrhagic inflammation of the dura mater!'" As an example of bad medical jargon this would

take some beating, and the judge, who had professed to ask his question for the assistance of the jury, was visibly perplexed. Medical men, when in the witness box, should be prepared to state their views in English intelligible not only to jurors but even to judges. That appears to be one medical lesson from this case. Another is this. When I was in the class of forensic medicine, Professor Littlejohn amused me by instructing his medical pupils not only as to the manner in which they should deliver their evidence but even as to the clothes they ought to wear in the witness box. The local surgeon in the case which I have been describing cannot have been a Littlejohn graduate, since I find I have described him in my record as "a most remarkable figure. Dressed in a knickerbocker suit, brown shoes, a deer-stalker, a white shirt, white collar, *and* white tie, he looked like a cross between an English non-conformist divine and a professional bicyclist." Here again, the jury took a merciful view and found a verdict of culpable homicide. The amiable-looking elderly gentleman got eight years penal servitude. Although I would not myself venture to give sartorial hints to doctors preparing to enter the witness box, it was brought home to me quite recently that a becoming appearance is still an essential ingredient in successful evidence. One of our judges told me, in enthusiastic terms, that a doctor who had just appeared before him had been (I quote his actual words) "the best witness I ever heard in a court of law." It happened that I too had heard the witness, at least in part, and had been suitably impressed myself with the fact that the doctor in question had well-turned ankles and was sensibly wearing a brand-new pair of nylons for the occasion.

It has been suggested to me that some medical men are reluctant to figure in the witness box because they are thereby exposed to being bullied in cross-examination. This is not in my view a valid objection, since no cross-examiner, however formidable, should have any terrors for a witness who is speaking I don't say the truth but what he genuinely believes to be the truth. Sometimes witnesses bring trouble on themselves by arguing with counsel, or trying to be "clever"—always a mistake—or by answering the wrong question; but proper cross-examination (and improper cross-examination will soon be stopped by counsel on the other side or by the judge) still remains the most satisfactory check yet devised on a witness's truthfulness. The point which I want to make now is that, contrary to the popular impression, examination-in-chief is certainly much more important than cross-examination, and almost certainly demands a higher standard of technique, both in counsel and witness. This was told me many years ago by Condie Sandeman, himself a great master of both arts; whether I should by now have discovered it for myself by the inductive method I am not in a position to say. A witness of course is first examined in what he has to say by the counsel on his own side—this is called examination-in-chief; and is then cross-examined by counsel on the other side. In examination-in-chief the

examiner should elicit the evidence without asking "leading questions." (A leading question is one which suggests its own answer.) If he is driven into asking one, counsel on the other side will insist on its being noted as "Q. and A." and the value of the evidence is seriously discounted. In examination-in-chief the examiner is painting the picture which he will afterwards have to exhibit to the judge, or the jury, and later still to the court of appeal, civil or criminal. The true artist will be able to point to a logical, connected narrative, unbroken by the "question and answer" which would indicate that he has been forced to ask a "leading question." Now it is here, obviously, that a medical witness who knows his business can be of enormous assistance. Without being discursive, he should never hesitate to give reasons for his views as he goes along, and so obviate the necessity for the examiner to suggest his reasons to him. I still recall with admiration the evidence given in a long and troublesome nullity case in which I was one of the counsel. Like all such enquiries it was of a delicate and difficult nature, and the period to which it related was so remote that much of the evidence seemed archæological rather than gynæcological. This doctor seemed to know by instinct what the examiner wanted to elicit next, and with almost no prompting presented a connected and convincing piece of testimony which went far to ensure the success of his side.

"Never volunteer evidence" says Taylor's textbook, but that rule is stated far too widely and must be applied with caution. Always be sure to see that everything comes out in chief which you have got to say. Never "save" anything for cross-examination. An amusing example of the neglect of this rule occurred in the New York courts, and also serves to illustrate, what I have already mentioned, the fatality of being "clever." In a murder case the defence of insanity was tabled, and Dr Allan McLane Hamilton, the most eminent alienist in New York State, was called to support it. The defence lawyer thought that Dr Hamilton's evidence would emerge more tellingly in cross than in chief and contented himself simply with asking the witness if he had examined the prisoner, and if so what he considered to be his mental condition. "Insane," said the doctor. The next passage I take from Wellman's *Art of Cross-Examination*. "'You may cross-examine,' thundered Howe, with one of his characteristic gestures. There was a hurried consultation between [the district attorney] and his associates. 'We have no questions,' remarked Mr Nicoll quietly. 'What!' exclaimed Howe, 'not ask the famous Dr Hamilton a question? Well, I will' and turning to the witness began to ask him how close a study he had made of the prisoner's symptoms, etc.; when, upon objection, Chief Justice Van Brunt directed the witness to leave the witness box, as his testimony was concluded, and ruled that in as much as the direct examination had been finished, and there had been no cross-examination, there was no course open to Mr Howe but to call his next witness!" Wellman



counsel, a doctor hates to be discredited, yet usually he has only himself to blame.

Dictators in jack boots and peak hats cut powerful figures, criminals when stripped naked lose all courage. Our predecessors of the nineties and even later created a presence with their cravat and frock coat of varying cut which must have greatly enhanced their confidence in giving evidence. Now the Bar alone maintains a picturesque appearance in wig and gown. Would it not be reasonable to expect our valuable services towards achieving justice throughout the years to be rewarded by some distinguishing attire. Some may have better ideas than a wig of pale pink and a tie of red, but at least such might be pleasing to the Minister of Health and make a greater number of doctors feel at home in the witness box.

The historical relationship of our two professions probably dates back to Moses or beyond, at least he had vested in his own person all the necessary qualities. Instances abound of single individuals being admired by both law and medicine whether he be lawyer or doctor. What lovable or special quality did these people possess? Reputation and integrity no doubt, but not necessarily what we now call leaders of the profession. The something else may be difficult to discern but we should look for it in the hope of finding an outstanding pattern. A man famous in the Edinburgh Medical School in the middle of the last century was Sir Robert Christison, the medical jurist, and of him the Lord President Inglis, the greatest Scottish judge of the same period, said: "The professor went into the witness box not in the spirit of a partisan but in his proper office as a medical jurist, to aid the court and the jury in the elucidation of truth and in securing the ends of justice."

Sir Edward Marshall Hall the colourful English counsel was the son of a doctor and made himself an authority on *materia medica*, putting this knowledge to repeated use in his trial work. Similar examples will readily suggest themselves to everyone. What then do we gain from a study of such careers. Surely it is this that their platform has four strong legs. Enquiry, judgment, memory and eloquence. The best medical witness has these four well-developed faculties. All of us inherit intelligence in variable degree; that cannot be altered, but a mind may be consciously trained to acquire and to grasp facts. "The purpose of education," said John Buchan, "is to train the mind and not crowd the memory," and so comes judgment which is so much more permanent than mere wit; wit resembles a picture drawn in the sand, quickly formed, easily obliterated. Judgment is like a sculpture in stone, made with difficulty but enduring. There is only one path leading to truth and that is the path of patience. The more ignorant a man is the more likely is he to be impatient. Both professions suffer at times from this to the joy of the press who finds that mud slinging makes good copy, raising doubts among the trusting public, since it is sad but true that each doctor by the evidence

which he gives in public and the manner in which he gives it, improves or tarnishes the reputation of the medical profession much more so than does any of his activities in private practice. Memory comes with experience and thus is created the head-line for the editorial on "doctors disagree." Well they base their evidence upon their previous experience of other cases and the experience of one doctor differs greatly from that of another. X and Y represent the unknown quantities to a mathematician: the whole alphabet of the doctor in the witness box is made up of X's and Y's and in these circumstances the wonder is not that doctors disagree but that their views can usually be reconciled with so little difficulty. The faculty of memory really requires few words—those who carry water in leaky buckets soon lose it, and those whose memory is defective soon lose their knowledge.

The fourth faculty, that of elocution, is rarely developed by doctors. As a race we doctors are probably careful, shrewd, and possessed of sound memories, but we are by no means capable of expressing our views promptly and convincingly in well-chosen words arranged in suitable sentences and in proper sequence. Too often we pretend to despise eloquence. We call to mind that shallow vessels make the most noise, that talkers are like trees with many leaves but little fruit, and we shield ourselves behind the fact that many of the most learned men in the world including Socrates, Plato and Aristotle have been notoriously incapable of fluent speech. This affected scorn helps neither the medical witness nor the party who calls him. Greater attention should be paid to elocution in the training of doctors. Eloquence enabled Caesar to quell armies, and in more recent times the Fuhrer and the Duce reached lofty heights by the same means, the most outstanding example of all being our own war-time premier. Such eloquence naturally has great persuasive value with a lay jury who are unable to grade scientific evidence according to its true probative value and in consequence they are more convinced by the persuasive or psychological appeal of evidence. Yet to the best advantage this must have the quality of terseness, but words must not be rationed to the extent adopted by that remarkable anatomist Dr E. B. Jamieson in his *Pocket Manual of Anatomy*, of which an American once said if one word were removed the whole book would collapse. Eloquence to be masterly requires a sensing of atmosphere, what we doctors like to call intuition. This was well illustrated here many years ago when an important case was being tried—a will made by a man who had been aphasic. A great authority on aphasia had given evidence at considerable length. Sir Henry Littlejohn, who had, I imagine, no more knowledge of aphasia than a first year student was then called. The judge, I rather think he was then the Lord President, said to Sir Henry, "the last witness has just said, Sir Henry—I wonder whether you agree—that when a man who is aphasic makes a will of considerable content it is advisable that an expert on aphasia should be present." "Most certainly my Lord," said Sir Henry.

"And why do you think so?" Bowing to the judge, the jury and the court, Sir Henry replied, "For the sake of the cloth my Lord." My impression is that this remark from Sir Henry possibly had a greater effect upon the jury than the learned pertinent evidence of the world-wide authority.

We owe a great debt to the legal profession for their almost invariable tolerance of our often too obvious distrust of court mechanism and regard the time spent as wasted. How tired they must get of our coming into the precincts of the court asking: Will you really need my evidence? How long shall I be kept waiting about? or I have an appointment in an hour and cannot possibly be kept waiting longer than that. We are never taught at an early stage to recognise sufficiently the nobility of the law or the respectability of its practitioners. An old writer said: "When justice dies let the world be made a bonfire," and Gilbert wrote: "The law is the true embodiment of everything that is excellent." A small girl was once struggling along carrying a very large baby. A kindly passer-by stopped the girl and said, "What a heavy burden you are carrying!" The child retorted, "Burden! He's no burden. He's my brother!" We must learn that the burden of giving evidence should be borne with the same good will.

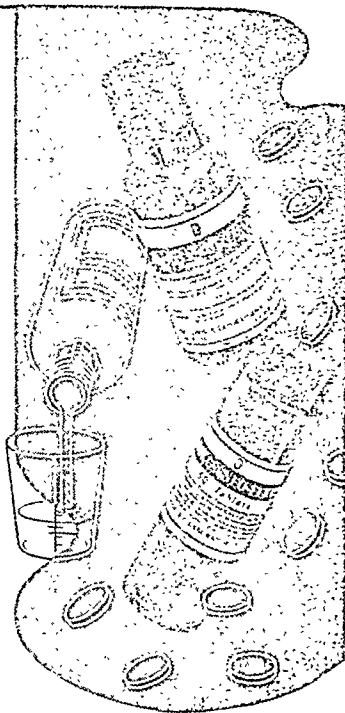
Few doctors realise that their services in the courts are even more valuable and noble than their services in healing sickness and delaying death. Few of us pause to think of the part played by law in civilised society. Without law princes lose their power and peoples their liberty; the rich are robbed and the poor are oppressed; travel by day becomes unsafe and sleep by night insecure; force reigns in the country and fraud triumphs in the towns. No man can enjoy fully either his life his home or his property. Inept words tend to obscure the breadth of the law-medicine relationships. Medical jurisprudence is one such term. It has been used to describe a variety of things, sometimes the application of legal doctrine to medical practice. The term forensic medicine has a nice ring and it is used to signalise the specialised applications of medical science in all varieties of legal proceedings. Perhaps the American synonym legal medicine makes the label sharper but raises an unwarranted inference that ordinary medicine may not be so legitimate. None of these terms conveys the true spirit or full content of law-medicine relationships which is in effect built up by many hands. Yet on our side the number who have contributed are a deplorably small proportion of the whole, and the time is long overdue when a remedy must be found for the future, since ever-widening fields of liaison are being opened up by the revolution in our affairs which is under way. Ignorance of the law is no defence, but now it is increasingly difficult to become conversant with two thousand new regulations annually, especially as our present legislators seem to formulate their edicts on the assumption that each of us is dishonest.

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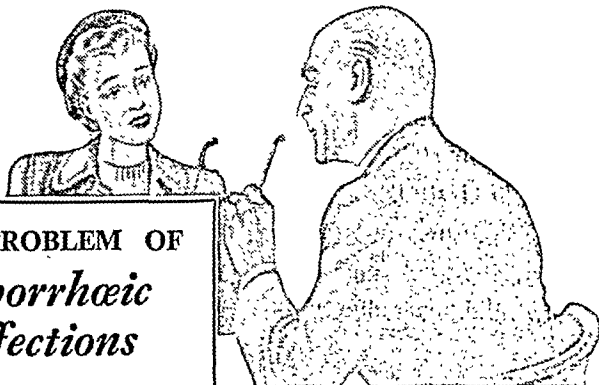


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How is a better training of doctors to be achieved, at what point should it commence, and what form should it take? I have given this question much thought and recognise that in one sense it is an individual matter which can only be dealt with by individual effort, but that breaks down when, as is seen, the tendency of the majority is towards evasion. A system is required which will expose each one to a recognition that in becoming a doctor he undertakes as a necessary duty responsibilities for the civilisation of the community that are not shared by other citizens. The remedy as I see it is to train the mind of the medical student in these matters from his first undergraduate year. Legal problems of medical practice would be presented in conjunction with specific subjects of the medical curriculum until the point arrived when the present brief class in forensic medicine would be regarded as a crystallising of the whole subject, rather than, as now, a rapid survey with perhaps undue emphasis on crime and toxicology. Ultimately the young doctor, like other people of scientific breeding, would come to realise that the law is social property and partly theirs.

It is appropriate to give a brief idea of what this might involve. Anatomy for instance provides an excellent opportunity of emphasising the legal aspects of establishing identity or as a subject of cross-examination in trying to discredit an expert witness. Physiology would deal with its own procedures such as "deception tests." Bacteriology could raise the legal aspects of blood group determinations and pharmacology has plenty of scope with narcotic laws and mal-practice in the use of drugs. In pathology the various liabilities of the clinical pathologist in cases of sudden death or in the examination of tissue at a post-mortem would be dealt with. When we come to systematic medicine and surgery the field opens out enormously with the main doctrines of the Workman's Compensation Acts, life, health and accident insurance, the law of damages and the law of evidence which the doctor as an expert witness should know, to say nothing of the surgeon's peculiar problems of operative procedures and his *bête noir*, the fracture. When we reach radiology, numerous aspects suggest themselves from a recollection of the increasing number of cases in which the humble film has become a decisive factor. Without labouring the matter further to consider the many specialities, including obstetrics and psychiatry, both of which present outstandingly knotty problems in everyday practice. Enough has been said to show that our student so trained would arrive at his graduation much better equipped to meet his unpredictable future at least to the extent that he will be less likely to develop and elaborate a legal-neurosis as his years pass.

Having attempted to disarm my King's Counsel with a rather discursive suggestion of infallibility—poor really, since no doctor is ever infallible except the psychiatrist—I would now like to offer some suggestions for improving our mutual collaboration. The law is well

aware that students of applied psychology have all manner of recommendations for revolutionising the so-called commonsense method of obtaining evidence which for so long has stood the test of time. Undoubtedly they have something to offer, but just as naturally much opposition will be met with until it can be established that change is not only desirable but universally applicable. For instance they tell us that scores of memory variations can be discriminated. Let your friends, they say, describe how they have before their minds yesterday's dinner table and the conversation around it, and there will not be two whose memory shows the same scheme and method. They urge that we should not ask a short-sighted man for the slight visual details of a far distant scene, yet it cannot be safer to ask a man of the acoustical memory type for strictly optical recollections. No one in the witness box to-day is examined to ascertain in what directions his memory is probably trustworthy and reliable. He may be asked what he has seen, what he has heard, what he has spoken, how he has acted, and yet even a most superficial test might show that the mechanism of his memory would be excellent for one of these four groups of questions and utterly useless for the others, however solemnly he might keep his oath.

Interest in this subject has grown and spread ever since the first of the carefully rehearsed scenes in the professor's class-room revealed so many variations of answers among the class who were witnesses, the greatest departures always being towards omission and falsifying. More elaborate and more ingenious tests and experiments never fail to show similar errors, but it seems even now that much more is needed if the psychological laws involved are really to be cleared up to the point where their claim for recognition by the courts can be upheld and prove the Scotsman's justification—"Thou hast loved righteousness and hated iniquity."

Forgetting the odd ways of psychologists for the present and turning to other practical matters resulting from one's own experience I have felt strongly that the manner of employing medical experts requires revision. The debate in the House of Lords on the death penalty brought forth out of the mouths of bishops some slightly slanderous statements about opening the door to the opinions and influence of more medical men and more psychiatrists. Whether the differentiation was accidental or studied I do not know, but it does seem to imply a distrust of us in erudite circles, which is not without reason when we consider the haphazard method which allows the highest bidder to call any evidence he may wish whether it be an unsavoury divorce petition or in pressing a compensation claim. Human nature being what it is no one need be surprised that such a system frequently produces remarkably prejudiced pronouncements. The responsibility of selecting medical testimony should rest only with the court and all payment made out of a court pool. A single risk being that the judge might select the wrong expert, but even this could be composed

by an obvious failure being black-listed. In all probability after such a system had been used for a few years it would be found that almost all medical litigation would be settled out of court. A further advantage would then accrue by removing the present impossible responsibility from the lay jury whose time honoured function looks a little archaic in this scientific age. What would P (a member of the public) think if he experienced the following treatment in a modern hospital? P goes into hospital suffering pain. Dr X says (testifies) that the pain is due to heart trouble. No one disputes him and the case is treated as one of heart disease. Assume, instead, that Dr Y examines P and says (testifies) that P is suffering from gall-bladder trouble. The hospital superintendent, desiring to resolve the conflict, calls in a layman from the street to say whether Dr X or Dr Y is to be believed, and on that basis disposes of P's case. P would be properly shocked at such a procedure because he would naturally expect that Dr Z an even greater consultant (expert referee) would be called into consultation to determine the true facts.

Thus it is that I press for the conviction that laymen cannot successfully try scientific issues. The layman is apt to import distorted notions of scientific matters into his judging process, and the warping effect is as pernicious whether he gives excessive weight to the evidence (augmentation) or too little (displacement).

Suggestions such as these if put into effect might rob counsel of some of his more joyful moments when skill and subtlty often seem to achieve unexpected triumphs, but I, no doubt in common with most of my fraternity, would be improved in confidence by not being interrogated on aspects of the Dangerous Drugs Act when it had little to do with the case or being challenged to disagree with Henderson and Gillespies's magnificent textbook on psychiatry when the statement in question was carefully removed from its context, leaving it applicable to a wide variety of conditions. Both these experiences are still sufficiently vivid to have left their mark on my pride.

Finally, let us hope that in the new order of society, where it seems that gold will be more valuable than mere man, we can still like to think of the affinities between our two professions forming a bulwark of sanity that will yet be a pattern of reasonableness for other sections of the populace to follow.

#### DISCUSSION

*Professor Sir David K. Henderson*, opening the discussion, said that the topic under discussion had taken a much wider aspect than he had expected, but it was a problem which psychiatrists came into contact with almost more than other members of the profession. Although their training is different, the lawyer and the doctor have certain objects in common—they both have it in mind to do what they can to help their fellow-men. They may have different ways of doing so but their aim is the same. The legal man thinks in terms of the welfare of society, whereas the doctor thinks in terms of how



to help the particular individual ; the doctor believes that conduct is instinctive and is determined by many unconscious factors, as well as by background and environment. He found it difficult in the law court to get the legal man to appreciate that a person might be unable to control his conduct any more than an epileptic could control his fit. The psychiatrist has been accused, or at least it has been implied directly and indirectly, that he is a soft-hearted sentimentalist. Recently Professor Henderson had been to a picture house and seen Hedy Lamarr in " Dishonoured Lady " in which she finds herself in the office of a psychiatrist. The psychiatrist in due course helped her to adjust herself, and then thought he would give advice to the villain. When the latter was leaving the psychiatrist's office he said to him, " don't you ever get tired of being the Almighty ? " That was a very apt remark, and conveyed a message. The tendency now perhaps is that the psychiatrist is expected to answer all the questions and to impress people with knowledge which he does not have. The tendency is to over popularise this topic at the present time, a tendency which Professor Henderson deplored.

Professor Henderson was particularly interested in Sheriff Simpson's opening remarks because he had immediately jumped into a discussion of criminal responsibility and quoted the case in which the words " a state of mental dissociation due to toxic exhaustive factors " had been used. Professor Henderson was partly responsible for this as he had appeared for the defence. In addition to the factors mentioned, Sheriff Simpson forgot to add that the man who committed the offence had been suffering from an attack of acute pneumonia complicated by empyema, for which he had been treated in hospital and had only been discharged a day or two previous to the offence. Professor Henderson felt he was justified in putting forward that defence and that it was not merely a fanciful proposition on the part of the psychiatrist.

Professor Henderson said he probably had the distinction of giving evidence in practically all murder cases during the last twenty-seven to twenty-eight years and felt he could talk with a certain amount of personal knowledge and experience regarding the medical man in the witness box. He had been treated most generously, not harassed too much and had always found an element of co-operation. It was not a question of taking sides but an earnest desire to get to the truth of the situation so that the accused person could get every chance. Professor Henderson believed that every criminal should have a chance of re-adjustment. More and more stress should be placed on environment and careful enquiry made into precipitating and mitigating circumstances. There is a certain amount of mental instability which does not amount to insanity but which indicates that the person is suffering from a certain disorder or a certain degree of instability whereby the charge of murder can be lessened to that of culpable homicide. This was a good differentiation and one favoured by Lord Alness. It was a new enunciation of the previous doctrine of partial insanity. This new plea of Lord Alness's was merely a suggestion whereby partial insanity was changed into something different and more weight was given to the mitigating factors.

Professor Henderson referred to the King's Park murder case, where a girl was murdered by a young man of twenty-three. He had been carrying on his work in the ordinary way. He had met this girl, had a few drinks, and went for a walk. The detectives came to his house at 3 a.m. and asked him about it. He admitted to it and took them to the place. It was apparently a motiveless crime. When examined he was able to give accurate details of

what had taken place. Investigation proved that from the age of five or six he had been a turbulent strange fellow, indulged in erratic conduct and behaved sadistically towards his sister. His previous life indicated certain instability, although there was nothing seriously wrong from the intelligence standpoint, but his conduct and instincts were perverted. He suffered from frustration, and his conduct was so uncontrolled as to lead him to perpetrate a hideous crime. It was justifiable that Lord Alness should change the charge to one of culpable homicide as they were dealing with a person who was not fully responsible for his actions. Professor Henderson would like to see this attitude adopted in regard to sexual crimes. The common practice is to send them to prison, where no treatment is given. In time they come back into ordinary life and are a menace to society.

It was over points like these that Professor Henderson welcomed the opportunity of speaking in a friendly way at such a meeting as this. He felt there might be a medico-legal association where problems might be discussed. The lawyer has the advantage in court as the medical witness cannot answer back. The doctor has to be careful not to argue with counsel, and in many cases he does not get a chance to express his opinion fully and justify his point of view without a certain amount of ridicule being directed to him by an astute cross-examiner. It was sometimes very difficult under these circumstances, and that is why there was something to be said for the Brigg's Law in America whereby medical reports have been open to both sides.

Professor Henderson also made reference to the Glueck suggestion. In this suggestion there are two divisions—the guilt finding-phase and the treatment-phase. The legal man is responsible for the first and the medical man along with others might help in the second.

In Professor Henderson's view there should be no controversy between the legal and medical profession—their common object should be to do what is best for mankind.

*Mr J. F. Gordon Thomson, K.C.*, referred to three points which had interested him in the discussion.

(1) Professor Henderson had spoken about a system in Boston whereby the medical evidence in a case was produced in the form of a report which both sides could study and from which each drew their own conclusions. Mr Thomson's experience in connection with one of the few tribunals in this country where medical evidence is given in writing, namely, the War Pensions Tribunal, contradicted this. In pensions appeals a great deal of confusion arose because there was no opportunity for cross-examining on the medical evidence. The result was that at the end of the day the court was forced to deal with long medical descriptions without having the advantage of getting them translated into terms which the lay mind could understand. Cross-examination would have done this. Therefore Mr Thomson was chary about advocating such a system in this country.

(2) The second point was the question whether a medical man should go into the witness box and take one side or another, or whether he should act as an impartial adviser to the court. Two speakers had stressed the importance of the doctor being impartial. It was difficult to know what was meant by that. A lawyer was retained to consider a particular case on behalf of a particular person and it was his duty to put forward the best case he could for that person. The case might require medical evidence. Mr Thomson could see nothing wrong in the medical man acting as other professional

witnesses did. Investigate the case and then put forward the view best suited to that case. He was not being asked to go against his conscience or against his own views, and if after investigation he felt his evidence would not help his client he should say so. Professional witnesses in other professions do not as a rule take up the attitude that they themselves are judges of the merits of the case. They leave that to the judge or jury. Doctors should realise, as do other skilled witnesses, that there is nothing discreditable or unprofessional in giving evidence on behalf of their clients. even if at the end of the day they should find they have been on the losing side.

(3) Finally, it had been suggested that there might be some antagonism between advocates and medical witnesses when in the witness box. In his own experience, when appearing for the defence in weak cases in the Criminal Courts he had often received assistance from Professor Sydney Smith who was appearing for the Crown. Professor Sydney Smith and many other experienced medical witnesses were quick to appreciate what defence counsel was trying to get at and to give such assistance as they could within the limits of their duty to the court. A good witness always realised what counsel on his own side wanted to bring out and he ought to try to realise what counsel on the other side was trying to make him say. Mr Thomson did not believe that there was any antagonism at all.

*Professor Sydney Smith* was interested in the way the discussion had moved away from the original subject of the doctor in the witness box, and had led on to a general discussion of the relationship between law and medicine. Professor Henderson's interest was naturally in connection with the behaviour of persons, and of the mental state which influenced their behaviour; and no doubt a case could be made showing a mental cause in most forms of misbehaviour. The law, on the other hand, must pay attention to the question of punishment. Crimes of violence—and particularly sexual crimes—are on the upgrade, and whatever be the medical view, the public have an interest and must be protected from such crimes.

The question before the house to-night was the doctor in the witness box. There is a tendency for the doctor to go into the witness box with a feeling of apprehension: that was quite unnecessary. In Professor Sydney Smith's experience the medical man is treated with great courtesy. He is there to help the judge and jury with his special knowledge, and if he sticks to what he knows to be the truth he need have no fear; but he must be chary not to be led into making statements about which he is not sure.

Regarding the question of the administration of justice; it had been suggested that the more wealthy delinquent was able to get better expert evidence. If the case is being investigated by the Crown, they get the best advice obtainable even if the person is destitute. If the person's mind is in question, the Crown undertakes the examination, not for the purpose of punishment but for the purpose of getting the truth. If it was clearly understood that the aim of the courts is to get at the truth of the matter all these misunderstandings about doctors in the witness box would disappear. The difficulty arises where doctors give evidence for one side or the other. Professor Sydney Smith's view is that the medical man should never go into the box and take sides, and certainly when cited by the Crown he should be absolutely impartial.

In compensation cases, however, doctors may quite honestly give opinions at variance with each other. Just as a person may have a pain in his stomach

due to one or other causes which may not be ascertainable, so a fall of coal on the back may lead to a fibrosis or other local reaction or to a neuroses and the relationship to the accident may be a cause of dispute. When an accident results in complications there is usually a difference of opinion. If there is no certainty about the way in which one thing may arise from another, such a difference of opinion is natural. Where there are conflicting views, it is Professor Sydney Smith's impression that the judge is usually able to distinguish between dependable witnesses and those who are not dependable, and so to guide the jury in their decision.

*Dr Harrowes* discussed the question of criminal responsibility and quoted from the evidence of the commission established in Sweden to set up a new penal code in so far as this dealt with the question of responsibility.

*Sheriff Simpson* and *Dr J. K. Slater* replied briefly.

## PSYCHOGENIC PAIN

By R. G. GORDON, M.D., D.Sc., F.R.C.P.Ed.

Physician Royal United Hospital, Bath

THE recognition of psychogenic pain as an entity in clinical medicine is nowadays almost universal among doctors but the explanation of its manifestation and the recognition of its exact nature is still obscure. Such pains are regarded by some as "nothing but malingering" others describe them as "imaginary" while still others regard them as symbolic manifestations of states of mind (Halliday, 1941) without being very definite as to how the state of mind is translated into a pain. Perhaps the majority would agree with the definition that psychogenic pains are due to an intensification of discomfort founded on subclinical bodily derangements of structure or function in "neurotic" subjects induced either by alterations of muscular or vascular tone or by auto- or hetero-suggestion. The vague pains often of psychic origin which are so commonly referred to as "Rheumatic" are typical of psychogenic pain and have been fully discussed by Flind and Barber (1945). They point out that before a diagnosis of psychogenic pain can be established with certainty, the following criteria should be established.

(1) No significant somatogenic factor can be discovered by adequate examination and investigation.

(2) Even if some possibly significant somatogenic factor has been discovered, treatment along somatic lines over a reasonably limited period has failed to effect improvement.

(3) Positive signs of emotional conflict or instability are present.

(4) And finally as the therapeutic test, adequate psychotherapy which succeeds in removing the emotional conflict or instability, also removes the pain.

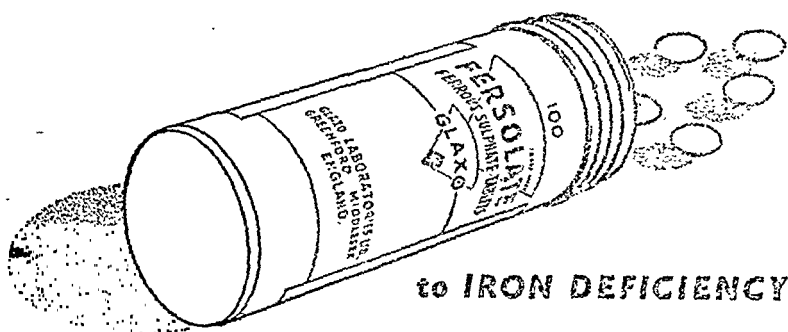
### THE NATURE AND PERCEPTION OF PAIN

It is desirable, however, to inquire further into the true nature of such pains. We must therefore, be clear as to the nature of pain in general.

Aristotle described pain as a "passion of the soul" and his view was maintained till the end of the nineteenth century. Pain was not thought to be a sensation with end organs, nerves and tracts like touch or heat and cold, but was thought of as a form of feeling akin to, but opposite to that of pleasure. From the beginning of the twentieth century, however, neurophysiologists have shown that pain is in fact a true sensation with end organs in the form of nets of fine branching fibres. From them proceed axons whose dimensions vary from very

A Honyman Gillespie Lecture delivered in the Royal Infirmary, 28th October 1948.

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thin to thick fibres. All these fibres enter the cord by the dorsal ganglia though by different peripheral routes. From the dorsal ganglia, fibres run in definite crossed paths in the cord, chiefly in the spinothalamic tracts situated in the antero-lateral segment, to the nucleus centralis posterior of the thalamus. From the cells of this nucleus relays go to the cortex, partly to the post-central area and direct and indirect connections are also made with the frontal lobes as is shown by the effects of frontal lobectomy.

Head's (1921) work following that of Roussy has shown that the ultimate reception area for actual pain sensations is in the thalamus and that at this level the subject is conscious of pain, though the localisation of its origin is not precise. Such localisation and the appreciation of degrees of intensity of pain and its nature is the function of the cortex. Lesions of the thalamus result in a raised threshold for pain but when the pain does get through to consciousness its intensity is increased. Such thalamic pain may reasonably be regarded partly as a feeling and partly as a sensation. The sensory character of such pain is shown by experiments on patients with a unilateral thalamic lesion when a stronger stimulus from the side opposite to the lesion is required to register pain, but if identical stimuli are applied to the two sides, provided they are above the threshold value, the stimulus on the side opposite to that of the lesion is felt more intensely than that applied to the same side. Nevertheless these thalamic centres concerned with the perception of pain are modified by emotional and even intellectual influences. Such influences are of course reversible and it is not to be expected that they will produce structural changes in the thalamic nuclei which can be detected post-mortem, however sensitive or insensitive to pain the emotionally instable may appear to be.

The paths by which the emotional and intellectual agencies affect the thalamic centres are clear enough. Le Gros Clarke (1948) has shown that the interconnections between the frontal lobes and the thalamus are numerous, and it is now clear from the results of lobotomy that by decreasing or abolishing these connections the agitation of the patient and the intensity of his emotional conflicts are diminished.

It is interesting to note in this connection that Freeman and Watts (1946) have advocated psychosurgery (lobotomy or frontal lobectomy) for the relief of intractable pain in organic conditions such as malignancy, primary or metastatic, tabes and the like. They explain that while the pain is not abolished by such procedure, the patient's responses are changed so that he no longer has any fear of pain and is therefore less disturbed and uncomfortable and suffers much less. It is manifest therefore, that the discomfort of emotional derangement is closely associated with the sensation of pain.

In support of the contention that pain is a specific sensation like other sensations and not merely an affective state, Weddell (1941) showed that in a patient suffering from a sciatic nerve injury it was possible to demonstrate an area of skin from which pain alone could be elicited,



no touch or temperature being perceived, showing that specific end organs and fibres do conduct pain sensation. From other areas such as the parenchyma of the brain, gastro-intestinal mucosa, etc., pain can never be elicited. The once commonly held theory that pain was induced by excessive sensory stimuli of other kinds was disproved by Adrian, Cottell and Hoagland (1931) who showed that stimulation of tactile end organs up to the capacity of the corresponding nerve fibres to conduct, does not elicit evidence of pain. The study of the mechanism of pain sensation shows that the somatic pain pathways via the sensory nerves subserve superficial pain which is of a burning or pricking quality and is accurately localisable. Deep pain impulses may approach the central nervous system in a number of ways ; some are conveyed by fibres attaching themselves to blood vessels part of the way and then joining autonomic nerves. Other fibres run with autonomic nerves and still others with somatic nerves, all these, however, enter the cord via the dorsal root ganglia. Deep pain is diffuse and aching and is much less accurately localised than is superficial pain. Superficial pain is sthenic and tends to elicit a reaction of fight or flight, while deep pain is asthenic and may induce nausea, fall in blood pressure, prostration and syncope and the total reaction will tend to be withdrawal, inactivity and rest.

The function of pain is not altogether clear. Pain is not the only warning of danger, indeed reactions to avoid danger are more often elicited by the other senses, vision, hearing, smell or touch, but pain may be a final warning of the imminence of tissue damage. Nevertheless severe illness or wounding is not necessarily associated with bad pain as was shown by reports of those seriously wounded in the war. Slight superficial wounds unattended by general or local shock are more likely to be associated with severe pain than those which have involved extensive tissue damage.

In whatever way sensory impressions reach the brain the perception of pain depends on the threshold of consciousness to pain. This may be defined as the least intensity of painful stimulus of which the subject is aware. Contrary to expectation the threshold of pain is remarkably constant in persons subjected to controlled laboratory experiments, and does not seem to be seriously influenced by differences of age, sex, various emotional states or fatigue, provided that the subject is able to maintain proper attention to his tests. It was, however, observed by Hardy, Wolff and Goodell (1943) that distraction, suggestion and hypnosis may raise the pain threshold by as much as 35 per cent. It was also observed that certain persons, during periods of fatigue, lethargy, suggestibility, prejudice or anxiety, were unable to focus on the experimental procedure and that the threshold varied greatly and was unpredictable. It was further found experimentally that in suggestible or prejudiced subjects, placebos significantly raised the pain threshold, whereas ordinary effective amounts of analgesics produced a minimal effect in raising the pain threshold. Normally

the subjects were found to be able to differentiate the intensity of pain sensation finely and accurately but some were found to be untrustworthy witnesses. These latter were characterised by their over-reaction to non-noxious stimuli and by their general anxiety and prejudice toward the experimental procedure. In other words they were of the psychoneurotic type. It is necessary to find some explanation of the uncertainty of results obtained, since most people would have expected that psychoneurotic persons would be found to be much more sensitive to pain than are the so-called normal, but these experiments show that they are not.

*The reaction to pain.* Wolff and Hardy (1947) have pointed out in considering pain that it is important to recognise the distinction between the threshold of perception of pain and the reaction to it. Although pain threshold is remarkably constant, the "alarm" reaction threshold varies widely from subject to subject and in the same subject from time to time. It is usually below the pain threshold although sometimes above it. This reaction is practically always initiated by painful stimuli but also by non-painful stimuli if the latter have become symbols of painful or dangerous experiences. Chapman and Jones (1944) found that "neurotic" patients in general displayed a lower threshold for reaction than did "control" individuals. This reaction component of the pain experience includes an important "quale" or feeling state, in this case unpleasant, and represents the individual's response to a given situation, based on his own past experience and inborn peculiarities. It is apparent therefore, that although pain is a specific sensation which can be scientifically measured and its threshold is remarkably constant, yet, because of its intimate linkage with strong feelings and other reaction patterns, the latter may be dominant in the experience and considerably modify the expected results, reactions to pain being specially modified by conditioning situations and firmly established beliefs. Experiments relating to the threshold of pain may therefore be misleading or confusing. The common analgesics in addition to effectively raising the pain threshold also have a major function in changing reactions, attitudes and feelings.

Symonds (1941) points out that the pain of a phantom limb may be due to an excessive stimulus from the periphery leading to a disorder of feeling tone at the centre. This particular pain sensation may therefore be not only a sensation of pure pain but a reaction to symbolical and direct reminiscences, not necessarily conscious, of a painful event when the limb was lost. The general unpleasurable feeling is therefore markedly intensified by such reactions. The same result is seen in the battle neurosis in which the reminiscences of terror, and such disorders of feeling tone as are experienced on the battlefields operate along with fear and anxiety relating to present conditions. These may well be expressed by complaints of giddiness, depression and palpitation, though the latter may not be accompanied by tachycardia, and also by experiences of pain. It is incidentally noteworthy, however, that

persistent terror may occasionally be the result of cerebral injury or softening without psychological trauma, and this may be accompanied by similar disorders of feeling tone and what is described as pain.

Thus, the evidence of recent research supports the old Aristotelian view that the "quale" or feeling state is, to the one who suffers, perhaps the most relevant aspect of pain. Yet it supports as well the conclusion that pain is a specific sensation with its own structural and functional properties. It becomes apparent that these two experiences of pain are not contradictory, for both go to make up the total pain experience.

In considering psychogenic pain therefore, just because we do not consider the stimulus adequate we must not dismiss the pain as "imaginary" and non-existent for the disturbance in "reaction" may be just as unpleasurable as is the actual sensation of pain, and this "unpleasure" is often described by the patient as pain.

We must admit, if we are sound physicians, that if a patient states that he suffers from pain, or what he describes as pain, he is suffering from a definitely unpleasant experience "painful" in the wider sense unless he is deliberately lying. True unabashed malingering is rare, if only because it is very difficult for a person to keep up the picture sufficiently continuously to deceive the trained observer or even his own friends and acquaintances who are always around him, and also because it is not often that the reason for keeping up the pose is sufficient to warrant the effort involved.

It is important, however, to remember that no pain, however much it may be due to structural lesions is ever absolutely constant and the variation in its subjective intensity will vary in accordance with, amongst other things, the direction of attention of the subject both to the source of his sensation and to the quality of the sensation of which he is conscious. The degree of pain therefore must always be difficult to assess and must not be used as a test of the patient's honesty. If the patient's interest is strongly engaged by something entirely outside himself his attention will be diverted from his disability and he will experience less pain. If on the other hand his interest is fixed on this disability his attention will reinforce the painful stimuli travelling from the periphery to the centre. Mere intermittence of the pain is therefore no indication of its nature or intensity.

#### HYSTERICAL PAIN AND THE PAIN OF ANXIETY STATES

Pain is generally described either as "organic" or "functional" but would be better distinguished as somatogenic or psychogenic. We may presumably describe as somatogenic, pain which is the direct or indirect result of painful stimuli arising from some structural lesion of any part of the body and such a condition may be reversible or irreversible. If this lesion is in skin or mucous membranes (superficial pain) the pain will be accurately localised to the lesion, if deep, *i.e.* in muscle, bone or viscera, it will be referred to the corresponding seg-

mental-somatic area as has been shown by Head, Lewis, Kellgren and others. Psychogenic pain on the other hand may be hysterical or the result of alterations of vascular or muscle tone or of glandular secretion directly consequent on autonomic disturbances. These autonomic disturbances may in turn be due to emotional conflicts which are the bases of many painful psychosomatic syndromes such as ulcerative colitis, and many cases of asthma and duodenal ulcer.

### HYSTERICAL PAIN

The nature of a hysterical symptom of whatever sort is immediately determined by a suggestion coming either from the environment or from the patient himself. Whether the suggestion works or not is determined and the resulting symptom is perpetuated, only if it serves the purpose of a complex or of complexes which are in conflict with each other or with the patient's whole personality. A complex may be defined (1922) as "a persistent but poorly organised or untidy system of emotional dispositions about an object which may or may not be capable of being represented in consciousness." To remove a hysterical symptom it is necessary to disentangle it from the complex so that it is no longer necessary or advantageous and to counter the originating suggestion. In order to make the "cure" permanent it is further necessary to resolve the emotional conflict which is disturbing the patient's personality.

In considering hysterical pain we may regard it as a release phenomenon and indeed this type of pain is almost always poorly localised and poorly graded in intensity. Such pain will recall the subjective phenomena of Roussy's thalamic syndrome. In this, it may be remembered, generally as a result of interference with the connections between the thalamus and cortex, the threshold of pain is raised but the intensity of pain experienced is much increased. Kendall (1942) has suggested that at least in some cases the inhibition comes from below rather than above, and that the fast-moving impulses travelling by the thicker pain fibres normally control and partially inhibit the slower moving impulses, travelling by the thin fibres. If, however, there is a lesion involving the thick fibre system this control and inhibition may be interfered with and the thalamic syndrome result. It is often the case, therefore, that any unpleasant feeling tone whether coming from the periphery or from higher levels of the cortex may be interpreted by the patient as pain. But confused unpleasant and painful messages from the cortex may be the result not only of structural lesions, but even more of emotional disturbances, complexes or false ideas which are part of cortical function.

Thus hysterical pain, while often originating from some actual structural lesion, frequently of a trivial nature, and perpetuated or intensified by being drawn into the service of a complex, need not necessarily originate entirely from association with such a structural lesion. It may be due to a misinterpretation of some purely psychic

unpleasurable feeling. Anxiety and guilt may often be less tolerable than pain so that these unpleasurable emotional states may be "converted" into pain, which may also satisfy the desire for self-punishment which is often felt by those suffering from pathological guilt feelings. This latter explanation will perhaps most frequently apply to headache. Hysterical headache is of a "thalamic" nature, that is to say it is poorly localised "all over the head," "generally on the top of the head" and so on and is poorly defined. As to its nature the patient will refer to it as "bursting, throbbing, sometimes shooting—I can't describe it." Deep pain from the head does not emanate from the parenchyma of the brain but from its coverings and from its supporting and vascular structure (Ray and Wolff, 1940). Especially is this so in respect of the pial and cerebral vessels. Ischæmia due to constriction of vessels in muscles is known to be attended by pain (Lewis, 1942) but constriction of vessels does not always cause pain and it seems more probable that it is their dilatation which is characteristically painful. It is notable that migraine due to dilatation of intracranial vessels is relieved by vaso-constrictors such as ergotamine tartrate. Pain may also be induced by traction on vessels as was shown by Kunkle, Ray and Wolff (1942). This probably explains why both increase and decrease of pressure of the C.S.F. is associated with pain and why headache may be induced by changes of posture. Headache is certainly not a symptom which is easy to describe exactly. Thus it was found that subjects could not differentiate the quality of headache whether this was induced by dilatation of cerebral arteries by histamine injection, by dilation of the branches of the external carotid in migraine, by traction on the vessels following spinal fluid drainage or by injection of hypertonic salt solution into the frontalis muscle while their complaints might vary as to site, pulsatile or non-pulsatile nature, duration or intensity. This suggests that the whole syndrome of headache is not under full cortical control. It has in fact become released from the cortical functions of integration, discrimination and accurate reference in time and place. Such a state of affairs easily establishes a vicious circle, for the longer the pain—which being "thalamic" is of increased intensity—goes on, the more fatigued will the patient become, especially if in addition his conflicts interfere with sleep or determine highly emotional dreams. The greater the fatigue, the less is he able to exert cortical control either in inhibiting the thalamic type of response or in managing and resolving his conflicts. Thus he may well drift into a state of confusion, apathy and hopelessness and continue to complain of pain in the head which, as the result of incautious remarks of the examining physician whose suggestions are readily accepted come to resemble more and more the headache associated with specific lesions; nevertheless such pain is really hysterical in origin though it may partially or wholly belong to that extensive group of diseases which are iatrogenic.

The pain which is associated with the anxiety states rather than with

hysteria is usually of the deep variety and is generally described as "rheumatic" if associated with muscles or bones. If visceral it is usually associated with an "organ," heart, bowel, sex organ, etc.

#### MECHANISMS CONCERNED IN THE PRODUCTION OF PSYCHOGENIC PAIN

As to the exact mechanism of the production of such psychological pain we may obtain a clue from the suggestions of Professor Henry Cohen. When dealing with the explanation of referred visceral pain, he writes (1947):—"From the endings of all pain nerves, visceral and superficial, there arises normally a constant regular stream of subliminal impulses which pass to the central nervous system. . . . Sarah Tower (1943) has observed spontaneous and rhythmic discharges in pain fibres and terminals of 1 to 8 a second, sometimes for hours. If this be accepted as normal, many hitherto irreconcilable observations on visceral pain can be reasonably explained. Ordinarily these impulses are subliminal; they do not cause pain unless disease lowers the threshold." (Or unless they are reinforced by other unpleasant impressions). "This reinforces the conclusion that there is after all an organic peripheral component of the pains which the hypersensitive neurotic feels all over the body. Pain impulses from a viscus . . . will pass the threshold if . . . supplemented by those impulses normally arising from homosegmental somatic structures so that they exceed the threshold value. . . . It is highly probable that pain impulses arising from the same segment will reach a functionally related area of the sensorium, and, when integrated with the cortical pattern of the body image by neural mechanisms at present largely unknown will be localised selectively in that segment." Cohen thus postulates a summation of stimuli from viscus and periphery (the latter of which are normal and constant) which crosses the threshold of consciousness so that a perception of pain is referred to the particular segment involved, or the organ associated with it. It is possible, however, that the same result may be obtained by the combination of the peripheral stimuli just above the threshold of perception with unpleasurable impulses coming "down" so to speak from higher levels as from those coming "up" from the viscera. As Cohen says we know that there is a cortical pattern of body image, and bodily areas are therefore related to ideas and images originating at high cortical (psychic) levels. This may explain the "symbolic" pains postulated by Halliday (1941). Emotional conflict relating to these "area images" may therefore determine perceptions of pain in definite parts of the body and have symbolic value. Thus to take a rather crude example, the thought that so and so or such and such a situation gives me a pain in the neck may be translated into actual cervical pain, especially if a mild degree of myalgia which is very common in this region of the body acts as a reinforcing suggestion and the subliminal stimuli coming from this area are operative. The threshold of pain or perhaps more accurately of

unpleasant feeling, may be lowered moreover, by the fatigue inevitably associated with emotional conflict, and the reaction to this "unpleasure" increased by the concentration of attention both spontaneous and voluntary on the area involved.

As to the diagnosis of such pain especially that referred to the abdomen certain axioms are useful. Alvarez (1946) has pointed out that if abdominal pain is described as constant with no intermissions it is generally psychogenic. Somatogenic pain is almost always intermittent varying in intensity but never completely in abeyance, while if there is a story of perfect digestion between attacks, then the attacks are in all probability psychogenic.

While somatogenic pain may begin in different places it always ends in the same spot, whereas psychogenic pain is not so closely localised at any stage of the attack. At the same time the description of pain given by patients suffering from structural lesions is definite and almost always expressed in the same words, while those suffering from psychogenic pain are indefinite and vague in their complaints. The description is often moreover grandiose and dramatic.

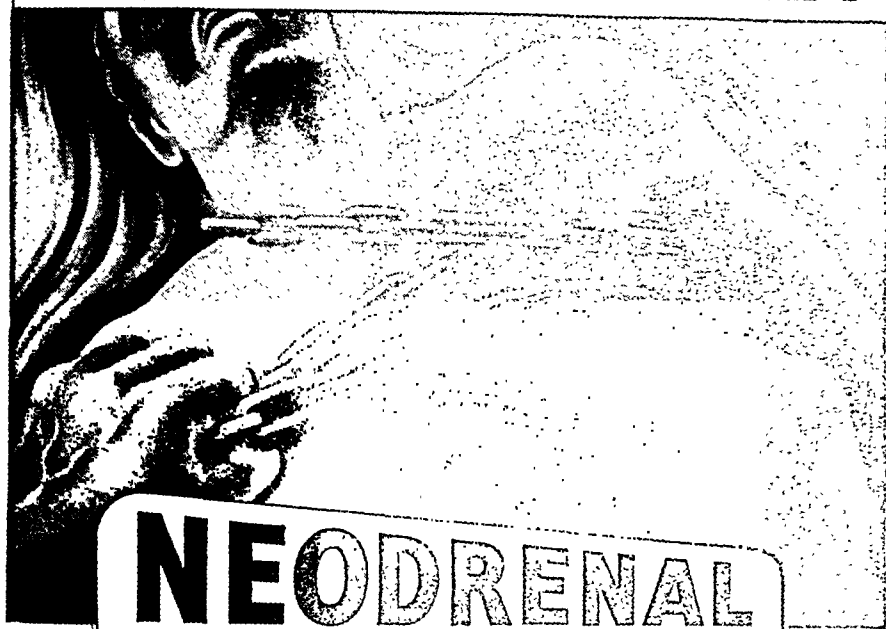
Pain which is not relieved by analgesics, even by morphia is usually psychogenic or at least there is a strong psychogenic overlay.

The spastic colon a common form of so-called "abdominal neurosis" which may be very painful, is a real entity and is almost always psychogenic in origin. It may be described as an unruly bowel which must be lived with, although it may be subdued or even made to behave properly if the underlying psychological disturbance can be wholly resolved.

In all cases of this type of psychogenic pain the trouble seems at least to the patient to originate in some definite and recognisable cause; though this will probably be found not to be adequate or in true logical sequence and therefore is not a satisfactory explanation to the physician or surgeon of the nature, severity or duration of the symptom. The pain may, however, last a long time and spread widely, because the stimulus, inadequate though it may be, is continuous and the central control and power of discrimination is relaxed because of fatigue or intervening disturbances such as those accompanying menstruation, pyrexia or anæmia. Sometimes pain and tenderness of this order may become widely diffused in consequence of the effect of debilitating psychical states, such as anxiety or emotional shock, quite apart from any physical ill-health. Neuralgia and superficial tenderness of dental origin not uncommonly assume undue proportions owing to insomnia, anxiety and worry, and it is well known that the mental state of the patient has a profound influence over pains originating in the pelvic viscera.

Occasionally the central resistance to potentially disagreeable impulses and the threshold to perception of pain is temperamentally so low that pain may appear without any obvious cause relating to peripheral irritation. Some women are rarely free from tender spots

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in various parts of the body, representing the maximal focus of one or more tender areas. These spots form centres from which pain may spread widely under the influence of suggestion or of emotion or other conditions which lessen the dominant power of higher centres. No gross visceral stimulus is required, though the areas may relate to "inferior" viscera using the word inferior in the sense of Adler's (1917) organ inferiority; the central apparatus is already in an explosive condition, and any relaxation of physiological control leads to an outburst of neuronal impulses manifested in widespread discomfort. In such cases the order in which the phenomena appear does not follow the usual manifestations of pain associated with organic visceral disease. Severe pain over the lower part of the abdomen and back may be accompanied by headache and tenderness situated over the forehead; the trunk can be widely affected without the head and neck or vice versa. Such want of harmonious correlation points to the central origin of these morbid phenomena; they are not the direct expression, however extensive, of peripheral stimulation.

Such changes of threshold or experiences of unpleasure may be brought about by vascular chemical or electrical changes in the brain. Alteration of blood supply either in the positive or negative direction will presumably produce their ultimate effects through variations in the oxygen concentration or in the other chemical constituents of the blood. Variations of  $\text{CO}_2$  concentration producing a shift of  $\text{pH}$  value to the alkaline side, such as is produced by hyperventilation, would appear to make the brain respond more easily to convulsive stimuli whether by reason of lowering the threshold or releasing the irritable areas from higher control. Similarly such agencies may facilitate perception of and reaction to pain and "unpleasure."

In the possible elucidation of the problem of how thresholds are raised or lowered or perceptions altered, attention must obviously be paid to the action of acetylcholin and cholin-esterases. Feldberg (1945) has reviewed the rôle of acetylcholin in central synaptic transmission. He concludes somewhat cautiously that although cholinesterase activity and acetylcholin synthesis, content and release within the central nervous system are of magnitudes compatible with the concept of acetylcholin mediation, nevertheless there are certain discrepancies in regional and special distribution of the ester and esterase which are difficult to rationalise. However, the action of "trace" quantities of substances in the blood stream may be of importance in this respect. Thus Zimmerman and Ross (1944) showed that the results of administration of 1 (+) glutamic acid to human subjects show a definite increase of efficiency, irrespective of chance or practice, especially in capacity to act intelligently. It has been known for some time that glutamic acid administration to rats increases the rapidity of learning to run a maze. The nature of the action of glutamic acid would seem to be related to the formation of acetylcholin thus facilitating impulse transmission. Conceivably other trace substances may inhibit such

impulse transmission. It is therefore possible that emotional changes especially those persisting for a long period may induce or be induced by alterations in the acetylcholin metabolism analagous to those produced by glutamic acid. Psychogenic pain of various types, may thus be associated with chemical changes in the blood even though such changes are apparently insignificant and only to be detected by the most delicate tests of chemical analysis. Such changes may set up vicious circles of facilitations of pain perception and inhibition of cortical control which can well account for the persistent but inco-ordinated complaints of those who suffer from psychogenic pain. All this, however, is highly controversial and cannot be regarded as in any way established.

Psychogenic pain which is so often the outward manifestation of psychosomatic illness cannot be easily classified and pigeon-holed so as to be attributed to this or that mental disease. In considering mental illness it is seldom possible to postulate one cause or to define particular disease entities, at least until they are well established in the course of time and as a rule we have to recognise a multiplicity of factors, hereditary, constitutional, endopsychic and environmental operating in varying proportions to produce the final clinical picture. Further, to quote Henderson and Gillespie (1947) it is necessary to take a longitudinal section of the patient's life as well as a cross section at any moment of time and to distinguish between the fundamental abnormality and the temporary symptom complex which it displays. We may speak of episodes arising in the course of a disorder such as hysterical symptoms in a schizophrenic psychosis or depressive periods in the course of a psychoneurosis, and pain may be the chief symptom of a number of conditions, but we must see the diseased personality as a whole before we can arrive at a true diagnosis even of the particular type of emotional reaction to which the patient is prone. Even in such a relatively clear cut clinical entity as general paralysis for example which we know to be due to syphilitic infection inasmuch as spirochætes can often be demonstrated in the cerebral cortex, we find a considerable variation of clinical manifestation on the one hand and of emotional reaction on the other. Some patients are depressed, some elated, some grandiose and some suspicious; some show preponderant mental deterioration and others physical failure, while probably not more than 2 per cent. of cases of syphilitic infection ever develop general paralysis at all. This can only mean that other factors, hereditary, constitutional or environmental must be operative and all these must be taken into consideration in assessing mental illness or its consequences. Again, so far as our knowledge goes at present there is no certain reason why anxiety, worry and emotional strain which are generally agreed to be the precursors of psychosomatic illnesses should produce asthma in one patient, peptic ulcer in another and ulcerative colitis in a third. There may be a hereditarily determined organ inferiority so that one organ or symptom is more liable to suffer from disease processes than

another. Adler (1917) described such organ inferiorities and sought to explain certain psychological anomalies as being the psychic equivalents of such abnormalities, but the reverse idea is even more probable that psychological anomalies possibly involving the cortical body image are represented by physical failures in the inferior organ.

On the other hand we may find organ tensions determined by specific emotional strains. Suggestions coming from others and from the patient himself may determine both the nature and location of psychosomatic conditions, while the cortical pattern of body image may be involved in an emotional disturbance. For instance, effort-syndrome is a good example of a psychically determined disability which may interfere very seriously with the patient's efficiency. It is characterised by infra-mammary pain, breathlessness and palpitation especially on exertion, which is not cardiac but of local origin in muscle or pleura, and as a rule by a conviction that he, the subject, is suffering from serious heart disease. It is not uncommon in such cases to find a family history of father or uncle having died of angina pectoris. If on the top of this the patient one day has a stitch in his left side after running or lifting something, which is merely a spasm of the intercostal muscles or an attack of intercostal fibrositis, it is not difficult to see that he may become seriously alarmed lest he himself has "strained his heart" and that he is in danger of death. Anxiety over this may stimulate thyroid activity so that he is prone to palpitation and readily becomes short of breath, and so the full-blown effort-syndrome is established. Similarly a relative who has died of cancer of the rectum may help to determine a spastic colon, or a case of phthisis, an asthma and so on. On such a soil it is very difficult for the examining physician not to implant further doubts or even certainties that the disease is serious. In such cases the doctor has a difficult and responsible task. He must realise that his patient is in a very real distress and must not dismiss his complaints as imaginary, for by so doing he will forfeit all confidence. At the same time he has to make it clear that there is no serious structural change and get the patient to understand that it is his mental attitude to life, and not his body which is at fault. This duty calls for much knowledge, patience and tact, and the doctor who is called upon to perform it is by no means to be envied, yet a successful issue is eminently satisfactory to all concerned, since it saves a great deal of invalidism and suffering. More complex, however, are the cases when the disability is transferred from one set of organs to the other. This is specially apt to occur in relation to the pelvic organs, for here the special reflex centres for bladder, bowel and sex organs are closely related both anatomically and physiologically and so the transfer occurs relatively easily.

Some examples may illustrate such conditions.

#### CASE HISTORIES

A. B. was an infantile masturbator and this habit resulted in very severe reprimands from her mother on whom, owing to the somewhat aloof disposition

of her father, she depended very much for the every day security of affection. From this beginning she developed an intense fear of and distaste for any stimulus of her genital organs and of her own sexuality. This fear was intensified by the discovery by her mother of her sexual play with a boy cousin, an exhibitionistic incident at school and other experiences not unusually met with in childhood. Being brought up in a markedly stressed religious atmosphere the conflict later involved and confused her ethical ideals and her relationship with God. The fear and disgust was not however sufficient entirely to repress the influence of her early stimulated genital segment for she developed a horrified interest in social work relating to sexual delinquency and rescue work, and an excited revulsion for the life class at the art school. She projected her feelings in an intense fear of and dislike of men as a class although she met many kindly, considerate and refined persons amongst her male acquaintances and friends. Her own sex life was unsatisfactory as she early fell in love with a much older married man of high principles who, although in the main a father surrogate was a good deal more besides. Feeling that any such attachment was morally wrong she violently repressed her feelings which repression drained her energies and to some extent disintegrated her personality. Even when later he became a widower and they were able to marry the practice of coitus interruptus did not help matters, and his early death prevented what might have resulted in the full consummation of a very real and deep affection. Here then we find a state of irritability and tension in the genital sphere which because of the intense endopsychic protective mechanism against any expression of her own sexuality, could not be expressed genitally but, on the basis of a very mild attack of dysentery, transferred itself to the neighbouring colonic segment in the form of a very painful and persistent ulcerative colitis. This only improved when the sexual conflict was reduced by an acceptance of the fact of the existence and normality of her own sexual feeling, though its gratification was still impossible. The pain was now transferred to a spasmodic condition of the muscles of her neck and back and it may not be too far fetched to suggest that the continuing tension expressed itself in muscular spasm and that having recognised her sexuality the conflict was now between the demands of this segment for gratification and the upright and strictly normal behaviour which she felt she owed her early training and the memory of her late husband.

Another case, B. C., may illustrate the spread from segment to segment in the pelvis. A very insecure young man having had certain homosexual experiences at his public school never advanced in his sexual development beyond this phase, though he was probably capable of hetero-sexual stimulation and activity. He could probably be most accurately described as a bisexual with a leaning towards homosexuality which was increased and intensified with use, until by the time he was 30 he was a confirmed homosexual. As with so many of his like he tended to glory in his sexual choice, stressing his æsthetic merit and used such specious arguments as to betray his insecurity which was also demonstrated by his reaction to his work and his home. He complained of intense burning pain and spasm in his rectum which after bowel movement spread to his bladder and penis. Similar but less intense anguish occurred after seminal emission. On examination no abnormality was found unless it was a definitely pleasurable sensation on stimulation of his rectal mucous membrane. He was definitely as the Freudians would say anal-erotic. After treatment the anguish was much diminished confined to the rectum and only really troublesome when the patient became anxious or

worried. He was also subject to an allergic sinusitis which behaved in very much the same way in relation to worry and stress.

C. D. was a strong-willed and dominant woman who lost her husband when her children were respectively 4 and 6 and so had to make provision for them. She started a school which she ran with some success, but it was never sufficiently prosperous to free her from financial anxiety. She ruled her staff and her pupils with a rod of iron and if crossed would fly into rages which led some of her associates to accuse her of sadism amounting to a perversion. In these rages her face got suffused with blood and after such attacks she complained of violent headaches. Her blood pressure rose persistently and the headaches increased as her life advanced and she finally died of gangrene of the foot, to relieve the pain of which she had to receive large doses of morphia in the last months of her life.

These examples may show how emotional stresses may induce painful states which may make the life of the patient quite unendurable and may ultimately even be followed by irreversible organic changes. In all three patients many somatic treatments were tried without any success at all and psychological treatment did not produce any quick cure. Indeed in the last case no psychological treatment was ever instituted, but in the first two cases considerable benefit accrued, strict attention being paid at the same time to the relief of associated physical symptoms. Obviously prevention of the establishment of a vicious circle would have been most effective for early, prompt and energetic treatment is as necessary for the cure of mental illness as it is for physical illness. Irreversible mental changes may take place with the passage of time as do irreversible physical changes and in the present state of our knowledge we cannot expect 100 per cent. success with psychotherapy any more than with any other form of treatment. That however is no reason why we should not expect a considerable measure of success in relieving psychogenic pain if the case is correctly diagnosed at an early stage of the illness and energetic treatment is undertaken from all angles, for no one panacea is likely to cure or indeed to benefit for long, a patient whose whole personality has become disorganised.

#### PSYCHOLOGICAL ASPECTS

From the psychological angle we must remember that for the development of a psychosomatic disorder there are three requisites: (1) a psychoneurotic predisposition; (2) an exciting emotional conflict; and (3) restriction of outward expression of the conflict. All individuals, whether normal or psychoneurotic, seek relief from the mental suffering occasioned by disturbing life problems. When emotional tension is expended by outward expression, muscular or verbal, all is relatively well. By taking some form of action or doing something about it, the individual "gets it off his chest" and feels better, even if he or more often she only has a good cry about it. But if emotional dissipation is constantly restricted, the tension gradually mounts and, in a psychoneurotic type of individual especially, the development of somatic

complaints including "pain" may be the eventual outlet and therefore even pain may serve a purpose. With the emergence of bodily symptoms the psychoneurotic tends to focus his attention on them and thereby is partially relieved from his inner mental tension. Although the psychophysiologic mechanism by which psychic disturbances are transformed into physical symptoms is not fully understood and is complex, the foregoing studies suggest that emotions produce their effects through the autonomic nervous system either directly or by way of the endocrine system, thereby producing increased muscle tension, vasospasm or metabolic changes including alterations in "trace" substances in various organs and structures, but especially in the nervous system. A vicious circle may thus easily be set up, the nature of which may be difficult to detect and still more difficult to break.

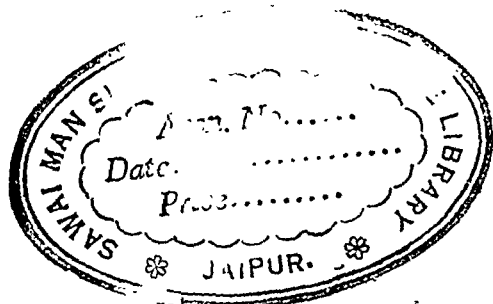
In the treatment of psychogenic pain therefore we have to consider what is the real origin of the mental disturbance which has caused the alterations in balance of function determining the pain. We must study possible origins of true pain sensations and treat these. We must also consider the emotional state of the patient, both conscious and unconscious which may give rise to distressing experience and over-reaction. We have in fact to attack the whole complex tangle of emotional and bodily responses which have been built up and we can only do this by getting down to fundamental causes.

To sum up it is suggested that psychogenic pain results from a combination of subliminal stimuli via the specific pain endings, fibres and tracts with unpleasurable impressions which, to use Aristotle's term, are passions of the soul. The proportion of these two components varies from case to case but it seems probable that wherever pain is a prominent feature of the patient's complaint both components are present. Therefore both will have to be treated to obtain an optimum result. Pain as a symptom can never be neglected or the confidence of the patient who suffers from it will be forfeited. Nevertheless the significance of the symptom may be very hard to determine, yet the reputation of the doctor may well depend on his success in this quest more than on anything else in medicine.

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# ARGUMENT ON NEURAL TUMOURS AND THEIR ALLIES

By W. F. HARVEY, M.A., M.B., F.R.C.P.E.

Director of Histological Research

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## PART III

"Ohne genaue Berücksichtigung der Entwicklungsgeschichtlichen Thatsachen entbehrt die Geschwulstlehre ihrer wissenschaftlichen Unterlage." (Marchand<sup>105</sup>).

### ASTROCYTOMA. ASTROBLASTOMA

FIG. 19.—*Astrocytoma*.—Showing several large swollen cells with homogeneous or finely granular cytoplasm and excentric nucleus. Nuclei when not pycnotic are diffusely and finely chromatinic, but there are parts in which there is a typical neurofibrillar feltwork separating the discrete astrocytes. Blood vessels are not seen and, in any case, are few. There are no mitotic figures. C.G., N.S., S. 18, N. 192.

A choice has been made of this illustration not because it is a typical field, which it is not, but because the large, probably degenerative, cells are very characteristic diagnostically and at the same time might from their size, lead to an error. If it were not for the excentric nuclei they could be mistaken for ganglionic cells, so that the tumour might be named a ganglioglioma. These cells could not be mistaken for macrophages.

The astrocyte and the oligodendrocyte are the most differentiated of the glial cells and represent a sequence of development—neurogonium, bipolar spongioblast, astroblast, astrocyte—which is distinct from the ependymal epithelial series. The oligodendroglia ranks with the astroglia as the supporting tissue of the nervous system and these with their opposite the epithelial ependyma make up the glioblastic as distinct from the neuroblastic elements.

In swollen cell regions of the astrocytoma the tissue lacks, or has lost, the typically abundant neurofibrillar matrix, the matrix which, together with comparatively low cellularity, gives much of the diagnostic character to this the benign tumour of the brain. If, however, the tumour is cellular and still of astroglial type, it may be denominated astroblastoma, where mitoses may be present and where short cytoplasmic prolongations may be directed axially from the cells to form a glial crown to a blood vessel. A more general designation is *glioblastoma isomorphe*. Direction towards blood vessels of the main cytoplasmic process is characteristic of the astroglia and the end of the fibre forms a podic expansion called a sucker foot. Astrocytes and astrocytomas are divided into protoplasmic and fibrous according to the degree of development or fineness of the fibrils. They are still cytoplasmic. Similar fibrils of the periphery of muscle cells and of fibroblasts are grouped with these fibrils as neuroglia, myoglia and

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fibroglia : they have, as Mallory <sup>106</sup> showed, similar staining reactions. A sub-variety of astrocyte is the piloid type in which the fibrils stream out axially, hair like, from either or both poles of the cell and are contiguous to one another. Such a picture is, perhaps, at its maximum in the marginal zone of the developing neural tube, in the palisades of the neurinoma and according to Biggart <sup>104</sup> as " isomorphic gliosis " in the glial scars of the spinal cord.

It would be well to round off this discussion by mentioning the glioblast as an immature, polymorphic and rapidly growing cell form in the glial series. It gives (Fig. 9) the *glioblastoma multiforme*, the malignant tumour of the brain, and may have a varied composition. This idea of a composite pattern for central gliomas is expressed by del Rio-Hortega <sup>55</sup> when he uses the terms " glioblasto-astroblastomas, oligodendro-astroblastomas and astroblasto-astrocytomas."

### PARAGANGLIOMA. GLOMANGIOMA

FIG. 20.—*Carotid body tumour*.—" Woman, aged 39. Noticed after confinement a swelling inside throat behind tonsil. Sore throat and pain 10 days, which disappeared. Gradual increase in size with production of slight dysphagia." Biopsy : Showing " the specific structure associated with an adenoma of the carotid gland. The cells are fairly granular and when treated with solutions of chromic acid take the yellow colour of chromaffine cells. The sections show irregularly arranged clumps and rows of cells occupying the interspaces within a close capillary network." (Dr J. W. Dawson). The patient, not operated on, was still in the same condition and certainly no worse 9 years later. 6909/24 and 9124/33. Courtesy of Dr Douglas Guthrie.<sup>108</sup>

As one of our presumptive tumours of the nervous system we may accept the general name, originally given to this class of tumour, paraganglioma, by Alezais and Peyron <sup>109</sup> and thereby admit the possibility of derivation from one of the " paraganglia " of Kohn. The carotid body is sometimes treated, like the adrenal medulla, as a pure endocrine gland, but debate continues as to any identity of this body with the chromaffine autonomic nervous system and likewise its identity with the aortic bodies, the coccygeal body and the sympathetic paravertebral chain of ganglia. The early names of *Glomus intercaroticum* and *Glomus coccygeum* give one clue to the direction of argument. If we accept the designation of neuromyoarterial glomus (Fig. 8) for the painful subcutaneous tumour, there seems no great difficulty in going a step further and agreeing to compound the neural or neurocrine and vascular characters of these organs under one family name. An embryogenetic origin from the " versatile " neural crest helps to solve some of the morphological difficulties but leaves much of the functional difficulty still in dispute. Masson <sup>110</sup> in his argument as to the nature of the carotid body and the coccygeal body showed that the latter consisted not only of glomus cells but of a closely associated, very intricate network of nerve fibrils in a sinusoidal vascular setting. Historically, when dealing with the carotid body and its tumours, one must refer to the great work of Luschka <sup>111</sup> who

<sup>106</sup> pp. 117, 8.

<sup>104</sup> p. 20.

<sup>55</sup> p. 79

<sup>109</sup> (4).

<sup>111</sup> pp. 412, 413.

gave the intercarotid nodule the name *Glandula carotica* and compared it to the "axillary hearts" of fishes and reptiles. An extensive literature on this group of tumours of the nervous system is given by Bérard.<sup>112</sup>

The first tumour of the carotid body to be fully described and, incidentally, coupled with tumours of the medulla of the adrenal was that of Marchand<sup>105</sup> who, however, was himself uncertain whether to call the carotid body a gland or ganglion and escaped decision by calling it provisionally *Nodulus caroticus*. Another interesting point made by Marchand and continued by him<sup>113</sup> later, when dealing with chorionepithelioma, was that he did not admit the completeness of Virchow's description by cell type or tissue of all malignant tumours under one or other of the denominations, "Carcinom, Krebs, oder Sarcom," a remark which might be well pondered over, as preliminary to new nomenclature or classification.

In the illustration here given of a very typical case we see the sinusoidal vascular pattern and the aggregation of cells which have been variously called balls, cords, tubes and strands. A peculiarity which seems to me especially noticeable in this specimen, though not so obvious in my other specimens, is that of multinucleated giant cells. Actually, I think this is appearance only, syncytial but not symplastic, and that the cell membranes may be present but not well portrayed. I have not used ammoniacal silver impregnation to test Lison's<sup>29</sup> statement on Kultschitzky cells that "every substance giving a chromaffin reaction ought also to be argentaffin," although the reverse is not true. The encapsulated tumour is rarely, if ever, accompanied by symptoms, whereas hyperpiesia is a diagnostic feature of the phæochromocytoma of the adrenal.

Excellent clinical and other illustrations of the carotid body tumour are given by Keen and Funke.<sup>114</sup> A critical, historical review with delicate-coloured illustrations by Dr H. M. Russell<sup>115</sup> shows all the microscopical appearances. My own opinion of the tumour is that it may be described in one sense as glomangioma and in another as paraganglioma and that these names do not contradict one another. Chromaffinity, of at least partial degree, may also be admitted. The tumour would not seem to be functionally adrenergic. Mention may be made, casually, to resemblance of carotid body tumour tissue to that of penile, erectile, cavernous vascular tissue as illustrated by Harvey, Dawson and Innes.<sup>22</sup>

### CHROMAFFIN (PHÆOCHROME) SYSTEM

FIG. 21.—*Phæochromocytoma*.—"Man age 46. Ill for 5 m. with dizziness, headache and failing eyesight. B.P. 230/130 Feb. 1942. Arteriosclerotic. Admitted with l. hemiplegia and B.P. 250/150. Optic fundi showed advanced papillitis: suggested cerebral tumour. Died in 24 hours. At necropsy gross cerebral hæmorrhage and no

<sup>105</sup> pp. 547, 580.

<sup>113</sup> p. 553.

<sup>29</sup> p. 155.

<sup>22</sup> "Endothelioma," Pl. XXXIII, Figs. 75-77.

cerebral or hypophyseal tumour. Left ventricular hypertrophy but no dilatation of heart. Kidneys and renal arteries appeared normal. Gross atheroma of aorta. Adenoma of r. suprarenal. Is this a paraganglioma? " The tumour occupied both medulla and cortex at the middle of the adrenal. Report 1625/11.4.42/1254: A face was placed upon the material along its whole length and showed tumour, fairly definitely circumscribed, occupying the medulla of the adrenal and flanked on either side by normal adrenal structure. Sections show: 1. A paraganglioma of the medulla ("chromaffinoma"). 2. Very uniform cell composition; epithelioid cells with disposition on sinusoidal blood channels—endocrine type. 3. Some giant cell forms with correspondingly large nucleus. 4. Tumour fairly well demarcated by fibrous capsule from the cortical adrenal tissue which has comparatively normal architecture. 5. A large vessel with sclerosed media (arteriosclerosis) and calcified—the result, doubtless, of the hypertension affecting the whole vascular system. Other vessels are almost obliterated with intimal and medial thickening and thrombosis. 6. No mitoses. 7. Some lipoid vacuolation. Courtesy of Prof. Spence, Newcastle.

The term phæochromic signifies staining dark (*φαίος*, dusky, gray) with chromium salts. The reaction is one of affinity of chromium dioxide and adrenalinogenic granules: it was discovered by Henle.<sup>116</sup> In the adrenal medulla, which is a major derivative of the embryonic neural crest, we have the extreme example of sympathetic nervous system turned endocrine. A group of tumours belonging to this tissue and to its allies of the retroperitoneal region, comprises the neuroblastoma or neurocytoma, phæochromocytoma and ganglioneuroma, with admissibility of the carcinoid and the melanoma. It has its liaison with carotid body, coccygeal body and glomus tumours: it contains members giving either, neither or both chromaffin and argentaffin reactions. The phæochromocytoma is, for the most part, a benign, non-metastasising tumour and if it is lethal, *i.e.* distinguishing lethal outcome from "malignancy," it is probably so because of its effect upon the adrenal cortex. As a functional manifestation related to the neurocrine cells composing it we find evidence of adrenergic activity with symptoms of essential hypertension. Some of these tumours, however, are claimed to be truly malignant in the histological sense, as, for example, by McGavack, Benjamin, Spear and Klotz.<sup>117</sup> They submit in explanation of the absence of hyperpiesia that the malignant tumours are composed of immature, unripe stem cells and that in this malignant stage functional activity is neither developed by, nor to be expected in them. The early developing adrenal medulla is not yet chromaffin as Alezais and Peyron<sup>109</sup> point out.

The cells composing the phæochromocytoma are larger than the more primitive, less differentiated, almost wholly nuclear, unripe cells of the neuroblastoma. Some of the cells may be seen, even in my small illustration, becoming distinctively large to resemble ganglion cells with abundant cytoplasm, a very vesicular nucleus and a prominent nucleolus. There is on the whole uniformity of cell type with differentiation progressing and an arrangement which suggests a loose highly cellular character with a modicum of intercellular matrix or dendritic network instead of the cell-to-cell cementation of a pavement or mosaic. Granular content, presumably chromaffin, may be seen in

the cytoplasm, at least to as great a degree with the staining used as is shown in the normal adrenal medulla.

Useful reviews, introductory to this difficult group of tumours, are given in the Peyron series by Bérard<sup>112</sup> and by Azémar<sup>118</sup> with discussion, illustration and reference to a voluminous literature.

I should regard the phæochromocytoma or chromaffinoma, names which lay stress only on a colour reaction, as referable embryogénetically to the neural crest and as representing a possible stage in differentiation of a tumour beginning with the neuroblastoma and ending with ganglioneuroma. This is very nearly equivalent to the statement of Peyron<sup>119</sup> that the "sympathoma" (embryonal), the paraganglioma (adult) and the "ganglioneuroma" of the adrenal medulla "do not represent absolutely different tumour types but rather varieties of a common lineage." Incidentally, Henle,<sup>116</sup> who introduced the chrome reaction for its distinctive colour effect on the medulla of the adrenal, did not think so very highly of its diagnostic specificity when comparing adrenal with the hypophysis.

## ENDOTHELIOMA OR NEUROBLASTOMA

FIG. 22.—*Ewing's tumour*.—A boy, age 11, whom I saw in 1934 at the stage of diagnosis as osteomyelitis with discharge from an incision above the ankle, died January 1937. I reported on my sections of the amputated foot, one of which was a large transverse section to include, at 8  $\mu$ , both tibia and fibula. My written remark at that time (24.3.34) becomes retrospectively, of great personal interest and was: "The entity 'Ewing's tumour' has never established itself very firmly as an accepted one. A recent paper by Colville and Willis (*Am. J. Path.*, 1933, ix., 421-429)<sup>120</sup> puts out a rather astonishing diagnosis for the 'Ewing's tumour.' According to them it is a metastasis and is the 'neurocytoma' or 'neuroblastoma' of Homer Wright. This view has a very distinct bearing upon this tumour for I should not be surprised . . . that it is a neural tumour, a neuroblastoma. . . ." 135S, 9/24.3.34.

An eponymous title for this tumour is justified in honour of its discoverer and, as a temporary necessity, until majority consent can be obtained to its nature. My inclusion of this tumour among "allies" of neural tumours is explained by the strong and reasoned contention that in spite of age and duration of the patient's life, it may be a metastatic neuroblastoma from a primary tumour of the adrenal medulla or sympathetic nervous system and not a primary "endothelioma" of bone. It is interesting also to argue that this tumour may be that referred to by v. Hansemann<sup>121</sup> as "Adenoma endotheliale" of bone.

Its solid rosette forms, which may be compared with those found and illustrated by Homer Wright<sup>100</sup>; its undifferentiated, loose, uncemented cells and its short, non-canalised, epithelial-like cords which are not shown in my illustration, are not at all unlike the neuroblastoma morphologically. The component cells are, however, larger and more differentiated than the neurogonia of the neuroblastoma.

<sup>119</sup> p. 10.<sup>116</sup> p. 152.<sup>121</sup> p. 53.<sup>100</sup> Fig. 4, Pl. XLV.

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They approach rather the primitive ependymoblasts or even more, perhaps, the cells of paraganglia. The opposing doctrine is that which regards the cells as endothelial and the pattern of the tumour to be essentially sinusoidal, which would relate its vascularity to the sinusoids of the bone marrow. It has to be admitted that, again, morphologically, the pattern, either as cell or tissue, may readily be compared to many hæmangioendotheliomas. Perhaps we may have to fall back on the dictum that morphological identity is not necessarily morphogenetic identity. According to Murray and Stout<sup>122</sup> it is dendrite formation which serves to distinguish foundation cells of the neuroblastomas from the cells of the lymphosarcoma and of Ewing's tumour when grown in tissue culture.

I cannot claim any large experience of this tumour and none of the complete necropsy which would go so far towards settlement of the two wholly opposite views of Ewing<sup>123, 124</sup> and of Willis.<sup>125, 126</sup> If I took the most typical of my specimens as foundation for discussion I should undoubtedly be attracted by a neural hypothesis of origin; this would be based not so much on the undifferentiated neuroblastoma or medulloblastoma but on a more differentiated tumour allied perhaps to the ependymoma which I have already discussed or, even more generally, to the paraganglioma. My single small illustration is inadequate to support discussion and, in particular, while it figures something like a solid rosette, does not figure the short cords that are in the substance of the fibula. These cords are very striking: they are not canalised and therefore not tubes, not "Schläuche." These cords or balls of cells would when cut transversely give the solid rosette, the palisade-cell corona with prolongations completely filling the central area. Another illustration of this same tumour was given in "Debatable Tumours."<sup>22</sup> While on the subject, once again, of the "rosette," I would suggest that the "solid rosette" may sometimes be the stage antecedent to the formation of rosette with medullary lumen and internal limiting membrane and not, of course, the rosette of perivascular type. I have considered in these studies various types of rosette, a conventional term, which may receive names such as ependymal, chorio-ependymal, perivascular, solid, coronal and wreath rosette. I may add to these the rosettes due to new formation of gland acini or vesicles, the rosettes mechanically produced by stress in a cellular primordium, e.g. by the secretion or production of fluid, and artefact rosettes.

The alternative heading to this abbreviated study helps us to understand that the term "endothelioma" is also, like "paraganglioma," a family grouping rather than a genus or species of tumour. In the present connection it does offer a reasonable alternative to a tumour of neural origin. In conclusion it is well to remember that the remarkable radiosensitivity of this tumour is noteworthy both for diagnosis and discussion.

<sup>123</sup> pp. 360-364.

<sup>125</sup> pp. 686, 7; 864-8.

<sup>22</sup> Endothelioma, fig. 71.

## NEUROFIBROMATOSIS

FIG. 23.—*Neurofibroma*.—Section of tumour in a case of neurofibromatosis in which there was formation of numerous subcutaneous nodules. C.G., N.S., S 2/L.N. 2945.

Von Recklinghausen's <sup>97</sup> disease is characterised by multiple or massive tumours mainly distributed over, though not entirely confined to, the skin, and by the pigmented patches or café-au-lait spots which were first noted by v. Recklinghausen (p. 4). The relation of these neurofibromata to other tumour types is referred to by v. Recklinghausen but is more definitely brought out by express statements, based on neural crest embryogenesis, such as that of Ross G. Harrison <sup>127</sup>: "Likewise the other derivatives of the neural crest may give rise to neoplasms and accordingly we have a whole series of meningiomas, neuromas and gliomas, which are related in their origin to the melanotic tumours." One other quotation may be introduced here from the number that might be chosen: it is the conclusion of Rosenthal and Willis <sup>128</sup>: "The association of neurofibromatosis with paragangliomas of the adrenals is too frequent to be fortuitous."

The compound name neurofibroma leaves one in doubt whether the tumour is a neuroma or a fibroma, and the subject has been discussed by writers for at least 60 or 70 years. It must be confessed that on section of a tumour nodule it is often disappointingly fibrous, due doubtless to overgrowth of endoneurial and perineurial tissue. We may remember, however, that in first introducing another name for cranial nerve neuromata, the neurinoma (*νεῦρον*, nerve, or cord; *ἰς ἰνός*, fibrous vessel, strength), Verocay <sup>61</sup> expressly insisted on the neural origin of the fibres. It is as a neural tumour, or malformation, that I include the neurofibroma in this series and emphasise its essentially congenital, naeval character. The justified insistence on the participation and domination by fibrous tissue in the tumour make-up may be conjoined with the names of Mallory <sup>106</sup> who insisted on the similarity of fibroglial, myoglia and neuroglial fibrils and of Penfield <sup>129</sup> who thinks that Verocay was mistaken and regards the neurinoma as perineurial fibroblastoma and the fibrils as reticulin fibrils in the sense of Mallory.<sup>130</sup> The fibre neuromas proper are the neurinomas. I refer under this name especially to the sheathing tissue of the neuraxons and their myelin within the neurilemma sheath and to the specifically neuroglial, neurilemma cell. Stout <sup>131</sup> calls the neurinomas neurilemmomas. The neurilemmoblast and the fibroblast, as cell bodies, are not distinguishable from one another by stains. Patterns are very helpful in biopsy diagnosis of neurinoma—the fasciculation, the wavy fineness of the fibrils, the length and waviness of the nuclei, the palisading or echeloning of the nuclei, the presence of lipoid vacuolation in cells (pseudoxanthomatous), cytolytic areas and, of course, the relation of the tumour to a known nerve. Actual nerves and neuraxons are scarce. Exception might be made, however, in the case of the so-called stump neuroma, where amoeboid, pioneering

<sup>127</sup> pp. xi, xii.<sup>128</sup> p. 602.<sup>61</sup> p. 6 and p. 64.<sup>129</sup> p. 1303.

and lengthening axis cylinders seek a distal neurilemmal pathway directing them to a selective and successful termination. A discussion of this process for neurocytes and fibrocytes by Paul Weiss<sup>132</sup> and by Schmitt<sup>133</sup> provides much suggestive explanation for nerve and nerve sheath patterns. The artefact hypothesis of Isaacs<sup>107</sup> for neurofibrillæ should not be overlooked.

Cirroid, plexiform and pacinian neuromas are special types. The first of these is exemplified by the remarkable case of Brögli.<sup>134</sup> The pacinian type forms one part of Brögli's publication and is referred to by Thoma<sup>185</sup> in discussing the painful subcutaneous tubercle, *Tubercula dolorosa*, which need not always be a glomangioma. Neurofibromatosis or neuromatosis would require a volume. The present note is disjointed but may serve to point out some of the implications of the subject, and some of the important literature.

### GANGLIONEUROMATOSIS

FIG. 24.—*Galgioneuroma*.—There were multiple tumours of the skin in this patient. Section, showing many fully developed ganglion cells, some of which are degenerate, and an abundance of intercellular, sinuous, parallel fibrils—neurofibrils. I owe this specimen, an unpublished case, to Dr Colin Campbell, Edinburgh University. 8126/53.

The ganglioneuroma has been indirectly referred to under the headings phæochromocytoma (Fig. 21) and neurofibroma (Fig. 23). It is a tumour characterised by possessing at least some, and there may be many, fully differentiated sympathetic ganglion cells. These are large, with abundant cytoplasm and a characteristic spherical, vesicular nucleus and show prominent nucleolation. The intercellular tissue of these ganglion cells is occupied by a fusiform cell type which may, itself, be abundant or more frequently present as an abundance of neurofibrillar cytoplasmic sinuous, piloid processes. There is in places also the usual, delimiting, septate, fibrous tissue to tumour fields. Ganglioneuromas of the skin, as one of the many manifestations of v. Recklinghausen's disease, are rare but a number of cases have been reported. They are tumours of the sympathetic nervous system and are to be considered as another of the derivatives of the "versatile" neural crest. A noted case of this type was reported fully by Knauss<sup>136</sup> and an illustration of the patient, a female child of 8 years, who showed 63 ganglionic neuromas in the subcutaneous tissue of the trunk and thigh is given by Sir John Bland-Sutton.<sup>137</sup> A recent publication on the subject of ganglioneuromatosis is by Stout<sup>138</sup> who deals with 243 cases of which 8 were allocated to the skin. An extensive bibliography to this article is a boon to be appreciated. The statement that ganglion cells can multiply *in vitro* will also be noted. It may be remarked that v. Recklinghausen's disease is conceived in terms of multiple tumours and extreme illustrations of the condition are given in almost every textbook on pathology or oncology. It is well recognised, however, that if the neural crest may be called "versatile" so can v. Recklinghausen's disease with

<sup>132</sup> p. 173.    <sup>133</sup> pp. 3, 4.    <sup>135</sup> p. 676.    <sup>137</sup> Fig. 78, p. 143.    <sup>138</sup> p. 102.

tumours ranging through melanomata, fibromata, perhaps lipomata to meningiomata, gliomata, phaeochromocytomata, neuromata, etc.—the “neural crest family” of tumours for short. Nor, yet, need they be always very multiple. We have here I think, illustration of the naevoid hamartias, hamartomas and hamartoblastomas of Albrecht.<sup>3</sup>

### GANGLIONEUROMA AND GANGLIONEUROBLASTOMA

FIG. 25.—*Ganglioneuroblastoma*.—“A middle-aged woman who had an occipital craniotomy for cerebral tumour. Post mortem the tumour was found evenly enlarging the left gasserian ganglion roughly to about the size of a thrush's egg and travelling along the mandibular branch and also into the inner ear. Moreover the left upper deep cervical gland was completely replaced by the same neoplastic tissue.”

Showing a well differentiated large ganglion cell closely surrounded by smaller, uniform, medium-sized cells; disposed in solid alveolar fields which are separated by narrow strands of ordinary fibrous tissue. In some places neuro-fibrillar and fasciculate patterns appear. The picture as a whole is reminiscent of an embryonic sympathetic ganglion at an early stage of development in which there is a mixture of discrete differentiated ganglionic neurons, undifferentiated neurons and an abundance of undifferentiated satellite cells. Other ganglion cells were present in this preparation and also developing ganglion cells recognisable by their nucleus and nucleolation. There is seen an epithelioid pavement pattern in the tumour cell fields in places without obvious intercellular stroma and there is also the suggestion of a single layer, special perimeter of cells. Some of the tumour cells are in mitosis. Small areas of lipid, xanthotic cells make distinct but isolated appearance. Courtesy of Dr R. T. Cooke, Preston. 9605, 9918/41.

FIG. 26.—*Ganglioneuroblastoma*.—An old slide, without history, except that this was a tumour from the brachial plexus. It is a tumour picture identical in all respects with that of Fig. 25, except for the inclusion in the midst of a tumour cell field of a large, well-formed, transversely sectioned nerve. C.G., N.S., S 135.

I have been puzzled by these two tumours and especially to decide what name to give them. Evidently possible diagnoses of oligodendroglioma, neurilemmoma, paraganglioma and ganglioneuroma loom upon our horizon. They are strikingly alike, and I think assuredly the same as, the retroperitoneal tumour described by Robertson<sup>139</sup> which he named ganglioneuroblastoma; this is a very suitable name if we regard the ganglion cell, the leptomeninx, the oligodendroglia, and the trigeminal nerve ganglion (Hamilton, Boyd and Mossman<sup>11</sup>) as embryogenically daughter cells or daughter tissue of the neural crest (Hamilton, Boyd and Mossman<sup>11</sup>). The termination-blastoma gives the significance of malignancy as set out by Harvey and Hamilton<sup>140</sup> and separates the tumour from ganglioneuroma simplex. In the first of these two cases (Fig. 25) there was actually metastasis to a regional lymph node. Robertson<sup>139</sup> seems already to suggest (pp. 148, 149) the possibility of this tumour being one of the large mixed group of paragangliomata. He also, as del Rio-Hortega<sup>55</sup> remarks, places it equidistant between the neuroblastoma and the ganglioneuroma. These views are also elaborated by Fischer.<sup>141</sup> The “ganglioglioma” of the central nervous system has been dealt with by Courville<sup>142</sup> and the literature of tumours of the gasserian ganglion is set out in the Peyron series by Bérard.<sup>112</sup> Robertson<sup>143</sup>

<sup>11</sup> p. 231 and fig. 238, p. 232.

<sup>142</sup> p. 656.

<sup>139</sup> p. 151 and pp. 148, 9.

<sup>112</sup> p. 127.

<sup>55</sup> p. 121.

<sup>143</sup> p. 81.

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seems attracted, for a tumour of the floor of the 3rd ventricle and the optic chiasma, by the name ganglioglioneuroma.

### MELANIN, NEURONÆVUS, MELANOMA

FIG. 27.—*Melanoma*.—Woman, aged 70 years. Very pigmented wart from chest wall, present all her life. Enlarging and ulcerating 4 months. Showing a great variety of structure :—blister-like islands of loose cells within the epidermal band and embrasures of similar pattern at the base of the epidermis; pigmented epithelium and pigmented melanoblasts; non-pigmented fields of melanoblasts; melanophores in the corium. The condensed cellularity, numerous mitoses and nucleolation of nuclei proclaim malignancy, while the genetic relationship of tumour to epidermis and the tumour cell type suggest a carcinoma. 174/39.

The biology and chemistry<sup>144</sup> of melanin and melanotic cells should receive priority consideration in discussion of the melanoma, as a neural or near-neural tumour. Both the endogenous and exogenous pigment require explanation. Many articles and monographs have been written on the subject. All tumours are composed of cells in tissue combination and the melanotic cell ought to be treated, if space permitted, under the categories of: progenitor, precursor, producer, provider and receiver cell or of a cell "sui generis." The solution key to the melanoma lies in the nature and function of the melanoblast. Melanin as a chemical subject for discussion is often taken up at the hydroxyphenylalanin (tyrosin) stage and followed through dihydroxyphenylalanin (dopa), to the recently synthesised<sup>145</sup> dihydroxyindole from which melanin is formed by oxidation with, or without, the accelerative action of an oxidase system. It was Raper<sup>146</sup> who first suggested "that melanin production occurs by the oxidation in the air of 5:6-dihydroxyindole. . . ." This sequence may represent degrees of oxidation and the emergent definitive melanin as a polymerised phenol. It seems possible that the "melanoblast" contains dopase to transform dopa into dihydroxyindole, itself colourless and of small molecule compared with formed melanin. This pre-melanin, of easy passage from cell to cell, if transferred to the epidermal host cell could become easily oxidised to form black melanin. We may not assume that all melanin is black any more than that all black pigment is melanin. Even the coal-black pigment of the miner's lung is not as black as one might expect in thin layer. Melanin pigments in the human subject are sepia-, russet-, golden-coloured or in early stages colourless. Blue nævi, blue eyes and the blue-shaven chin depend for their colour on the depth of the melanin and the scattering of light. Many pigments contend, histologically, with melanin for identification and especially the hæmoglobin and carotinoid pigments. Perhaps we may exclude the carotinoid pigments as being lipoids from melanin proper: there would remain, however, a neural ganglionic pigment called melanofuscin, a chromo-lipoid, for debate in this connection. The wear and tear brown pigments and the siderosis of erythrocytes are also a problem.



Formed melanin is bleached by nascent oxygen, is dopa-negative, argentaffin as distinct from argentophil and iron-free.

I cannot here enter into argument, even were I competent, on the origin of the melanoblast. The occasion permits, however, of my overt adherence to a view which I once looked on with suspicion, that of Masson<sup>37, 42, 147, 148</sup>; the nævus cell is a neural cell and the malignant melanoma proper is a neurocarcinoma. Masson<sup>147</sup> has gone apparently some way along the road on which I am following him here by referring to melanoblasts as near-allies of the cells of paraganglia and "close to the phæochromocytes." It did at one time seem beyond belief that the epidermal cell should only be a host cell and that the melanoblast role should be one of restocking *in vivo*, but the mode of action had been already figured in the illustrations of Ehrmann<sup>149</sup> as long ago as 1885. The octopus-like processes of the melanoblast, perhaps analogous to the amœboid pioneer and successful neural processes of Weiss,<sup>133</sup> enfold the epidermal host cells. These host cells may be in a palisaded, basal, columnar, epithelial-cell layer, while their donor cells may be situated beneath the *membrana propria* of the corio-epidermal junction or more frequently interpolated between and cap-like to, the bases of the epidermal cells. The movement of melanin or pre-melanin is epidermotropic, to become situated firstly at the upper pole of the epidermal cell nucleus. Progress of the melanin is onwards more diffusely and surfacewards. It is well to take note that this is the direction of movement of the melanin both for epidermis and retina and not in the reverse direction, except perhaps as a result of clasmotocytosis. The melanoblast does not rank as a tattoo cell and the explanation here favoured provides easy explanation of the Langerhans' melanin. The Langerhans' cells may be either the cytoplasmic, dendritic processes of the melanoblast, the melanoblast itself, or the host cell melanin and account for the blurred pigmentation of the lowest stratum of the epidermis in the negro skin.

As to the nature and origin of the melanoblast we may here give it without the usual question mark as genetically one of the cells of the dermatropic dorsal fork of the neural crest, the "versatile" neural crest as Harrison<sup>127</sup> calls it. This view seems to have been accepted by experimental zoologists. The reference to the neural origin—and this has been expanded greatly by Masson<sup>37, 42, 147, 148</sup> and others—helps us to accept what originally proved difficult and controversial, the varied appearances of the benign and malignant melanomata:—the deep nerve-like fascicle spreading out fanwise into the upper corium as sheath cells and apparently terminating in epithelioid, nævus-cell aggregates ("hederiform") which may resemble the tactile corpuscles of Meissner, or Pacini and the end-organ apparatus of Merkel-Ranvier. Not only so but the melanosis of the meninges treated of by Virchow<sup>18</sup> and even the whorled pearls of the meningioma sometimes described as Meissnerian (Fig. 4 of this series), receive a

<sup>147</sup> p. 34 and p. 35.<sup>149</sup> Figs. 3, 5, 6 and 7.<sup>127</sup> p. xi.

possible explanation as neural patterns. Masson's clear cells ("cellules claires") are very like Paget cells, and Paget's disease, histologically, is very like melanoma. Actually well formed pacinian touch corpuscles are evident in the unique tumour of Brogli.<sup>131</sup> The "corps ronds" and dyskeratoses of Darier,<sup>150</sup> including Bowen's dermatitis may be tentatively placed in this group along with Paget's disease. One and all, these various cells and structures may be the product of neural crest cells whether choroidal, meningeal, dermal or epidermal in ultimate situation.

A frequent puzzle of my own in studying the melanomata was that although the tumour could, if epidermal, be conveniently described as basal-cell in character, the component cells were not really very like those of the tumour ordinarily known as basal-cell carcinoma. A high degree of nucleolation is often present especially in early malignancy. Melanoblasts are reckoned to be in the epidermis and a malignant melanoma may be a neurocarcinoma rather than a basal-cell carcinoma. Basal, and truly epidermal host epithelium, may be highly pigmented. When epidermal epithelium of the base is palisaded and columnar I would suggest that this is an organised, differentiated epithelium, exhibiting *continentia pigmenti* (Masson<sup>147</sup>) intended to last long, like the pigment layer of the retina, and that when it is present the *stratum germanitivum* proper of the epidermis lies superficially to and not among these pigmented cells. The *stratum germanitivum* in that case, and also the germinal cells of the primitive neural tube could differentiate in two directions: in the neural tube this would be on the one hand to ependyma or rods and cones and on the other to glioblast and neuroblast, while the mechanism might be of the primary evocator type illustrated by Schmitt<sup>133</sup> for the neural plate and neural groove. The *stratum germanitivum* of the chorionic trophoblast would, by similar argument, be syntrophoblast and give rise to differentiated, cubical cytrophoblast or Langhans' cell layer resting on the core of the villus.

This description or discussion has not touched the melanoma itself in any detail. The detail may be found in standard works. It will suffice to present the conclusion, as a meantime belief, that the nævus cell tumour is a neuronævus and that the true malignant melanoma is mainly a neurocarcinoma. The acanthotic nævus is probably epidermal; the cells are immature, non-acanthotic squames, but not basal epithelium; the pigment is patchy in distribution being contained both in melanoblasts and epidermal cells. It seldom or never develops malignancy, but if it does it is squamous. An amelanotic melanoma consists of melanoblasts which are unable to, or have not yet developed their destined melanin, an explanation applicable to the cases of the albino, the piebald coat and the normal coat markings of animals, vitiligo and xeroderma pigmentosum. The dopa-positive and dopa-negative reactions of Bloch<sup>151, 152</sup> are dependent on the state or

<sup>150</sup> pp. 289-300, figs. 73, 76.

<sup>147</sup> p. 19.

<sup>133</sup> pp. 15, 16, fig. 27.

activity of the melanoblast which is still one and the same cell whether it be apparently ectodermic or mesodermic in situation. I have made reference already to the views of Parker<sup>19</sup> and of Spaeth<sup>40</sup> and one could not conclude without a reference to the original works of Unna<sup>41, 153</sup> and the outstanding illustrated monograph of Dawson.<sup>34</sup> The literature on the subject, however, invariably grows in volume with re-reading, but one may mention here for its personal and historical interest the work on the amphibian melanoblast of Lord Lister.<sup>154</sup>

Malignancy and radiosensitivity of melanomas are important items in the reports on melanomas. As a tumour it is said to be radio-resistant and one might think that even to radiation of the shortest wave length (100 to 1-100th Angstrom units instead of 3000) melanin pigment might be an obstacle, but evidently this is not an acceptable view. Matthew Stewart<sup>155</sup> gives the warning that malignancy of melanomas "is to be assessed from their histological characters without reference to their melanin content." The amelanotic melanoma may be not only a benign nævus cell tumour but a malignant tumour of cells containing few or no pigment granules unless, as Kopac<sup>156</sup> contends, "the synthesis of these structures is rapid and can maintain pace with dilution resulting from the extensive proliferation of the cells." Clinical pigmentation, it should be added, may not be taken as the limit of tumour advance or of the necessary excision.

In order to clear myself of an accusation of dogmatism I should like to quote and to approve of the statement of Fischer<sup>157</sup>: "Das was man mit der Bezeichnung 'weicher Nævus' belegt, ist histologisch und wohl auch histogenetisch kein einheitlicher Begriff."

## DISCUSSION

This entire series of small essays is mostly an argument throughout and would seem to require little further discussion. There are threads of thought, however, running through the sequence which may need to be drawn together and expressed as the presentation of a belief. There may even be need as Gowers<sup>158</sup> enjoins, to make their meaning clear to oneself. It is with this in view and with clear appreciation of the dangers of word spinning, that I set out a final series of propositions:—

1. A unifying classification of neural tumours can be included within the groups:

From

TUBE	{	<i>Hylic</i> . . .	astrocytic, oligodendrocytic.
		<i>Lepidic</i> . . .	ependymal.
CREST	{	<i>Neuroblastic</i> . . .	ganglioneuromas, paragangliomas neuroblastomas.
		<i>Melanoblastic</i> . . .	melanomas.
		<i>Lemmoblastic</i> . . .	leptomeningiomas, neurinomas.

<sup>155</sup> p. 4.

<sup>156</sup> p. 423.

<sup>157</sup> p. 298.

<sup>158</sup> p. 4.

Primitive forms and mixed forms of these tumours are only to be expected. The "neurogonium" is the basal or stem cell. Neuro-, lembo- and melanoblastic looks like a "mixed" classification and a transgression of the canons of logic, but is simply the combination, for convenience, of two bases.

2. Melanoblasts are neural cells *sui generis*—(1) neurodermo-, (2) neuromeningo-, (3) neurochoroidoblasts. They produce and deliver melanin and, like histiocytes with their cytosiderin, may become overcharged with pigment and have it unmasked.

3. Neurogonia, like many other primordial cells, may under evocator action develop in spherical patterns or other aggregates such as the pearl-like whorls of the leptomeninges, the ball-like ("Zellballen") structures of the carotid body, the nævus-cell groups of the skin and even shunt systems such as glomera and glomeruli. It would not be a great stretch of imagination or argument to include here that conventional structure, the retroperitoneal or adrenal rosette in this group.

4. Another nerve tissue organisation pattern that is recognisable in tumours is the fascicle and the palisade which may represent the successful shepherding of "pioneer" cytoplasmic amœboid processes of glial dendrites or of the neuraxons of a nerve stump. The development of a podic expansion, a plate or an arborisation is index of attainment successfully of cytoplasmic objective.

5. Neural rosettes may be purely ependymal, or retino-ependymal and of epithelial nature or, as complex mesectoderm, have a perivascular arrangement.

6. Neural cells of neural crest and tube may exhibit epithelioid appearance in corium, choroid, meninges and central nervous system as seen in such tumours as leptomeningioma, melanoma, glomangioma, oligodendroglioma, carcinoid, phæochromocytoma and paraganglioma. They are not only sheathing cells (lemmoblastic) but may be parenchymatous; neurocrine when producing epinephrin, protective when producing melanin, insulating when producing myelin. Some of the tumours, especially carcinoids and melanomas, may be spoken of as nævus-cell tumours. That designation does not of course apply to neural cells alone, nor is the term nævus synonymous with congenital.

7. Ganglion-cell tumours proper are peripheral sympathetic tumours, ganglioneuromas, not tumours of the central tubal nervous system, but rather derived from the neural crest. The term ganglioneuroblastoma introduces the element of malignancy and should have as antithesis ganglioneurocytoma. Its recognition also implies recognition of the fact that some neurones can proliferate. The term ganglioglioneuroblastoma is too compendious, of doubtful existence, and probably not necessary.

8. The cells or cell layer called *stratum germaniticum* is a basal or foundation-cell layer but need not necessarily be implanted on a basement membrane. As examples I may refer to its situation

with respect to a differentiated columnar, basal-cell layer of the epidermis, the ependyma of a ventricle, mucosæ, or the cytotrophoblast of a chorionic villus. It is, however, the proliferative cell or layer for any tissue and for any tumour, benign or malignant.

I withstand the temptation to produce a *schema neurogenicum*, for that has been already well done by many authorities: del Rio-Hortega, Bailey and Cushing, D. S. Russell, Cox, Courville, Penfield, Hamilton, Boyd and Mossman, and others.

The argument may be unduly condensed but I have given throughout authority and page for further reference by the interested enquirer.

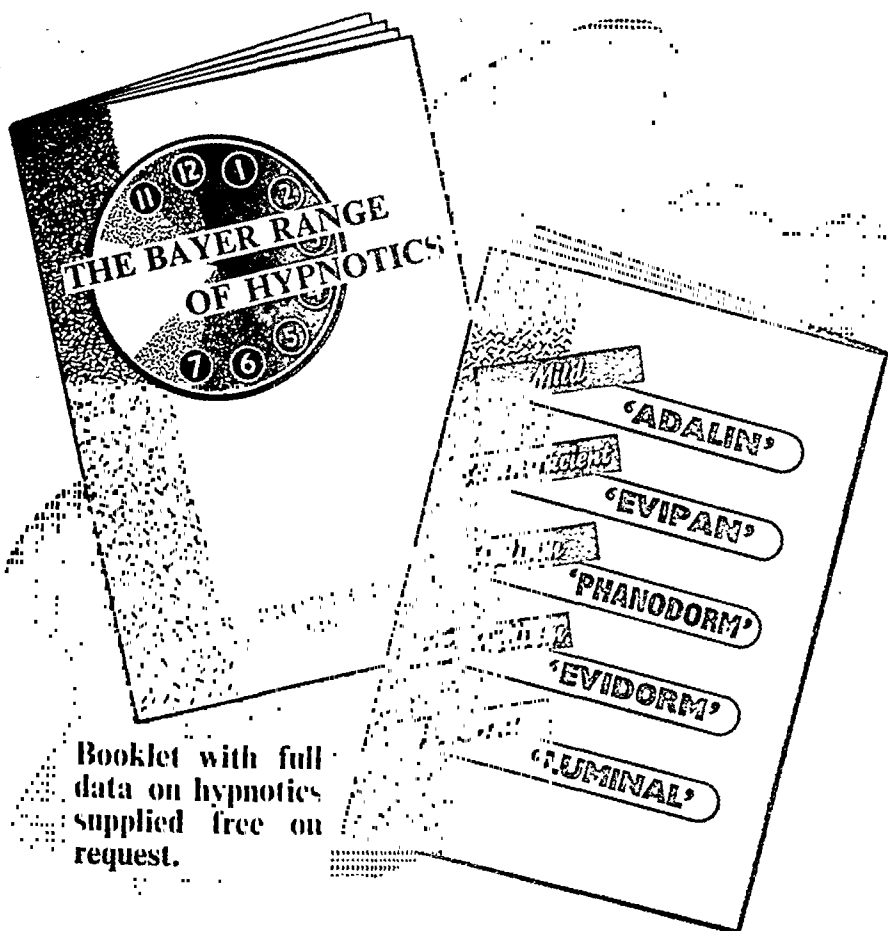
I am very grateful to the Carnegie Trust of the Universities of Scotland for generous help towards the cost of illustrations.

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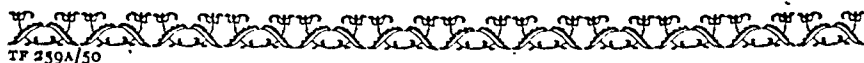


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## OBITUARY

### WILLIAM FREDERICK HARVEY

C.I.E., M.B., D.P.H., F.R.C.P.E., F.R.S.E., LIEUT.-COLONEL I.M.S. (RET.)

LIEUT.-COLONEL HARVEY, who died at Edinburgh on 11th September 1948, was born in 1873, the son of R. Harvey, M.A., LL.D. He was educated at Dollar Academy, and then proceeded to Edinburgh University. He also studied at University College, London. At Edinburgh University he took the M.A. degree, 1893, and then the degrees of M.B., C.M., 1897, with first-class honours. He obtained the D.P.H., Cambridge, 1899. After holding a resident appointment at the Royal Infirmary, Edinburgh, he entered, by examination, the Indian Medical Service, 1899. At the Army Medical College, Netley, where he studied preparatory to going to India, he was awarded, 1899, the de Chaumont prize in hygiene, the pathology prize and the prize for clinical and ward work. At Netley he became a pupil of that remarkable man, Sir Almroth Wright, for whom Harvey retained the highest regard throughout his life. Another distinguished worker who made a strong appeal to him was Professor Karl Pearson, Harvey having early appreciated the great value of mathematical and statistical methods in medical research. On arrival in India he served for the usual period in military employ. When this was completed he entered the civil department of Government and was appointed Deputy Sanitary Commissioner, Punjab, 1902-5. During his period of office he did important work on vaccination. In the Punjab, vaselin and lanolin had been employed hitherto in the preparation and preservation of the vaccine lymph, but Harvey, being dissatisfied with the results, introduced glycerin, after preliminary treatment with chloroform, for the purposes, and obtained much better results. He was selected for membership of the newly established Bacteriological Department (afterwards called the Medical Research Department) of the Government of India. His first appointment in this Department was that of Director of the Pasteur Institute of India, Kasauli, 1905-11. During his tenure, and along with his life-long friend, A. G. McKendrick, he investigated the preventive treatment of rabies; the results of their research had a fundamental influence on later work on the subject. Next he held the important post of Director of the Central Research Institute of India, 1912-26. During his Directorship the Government of India proposed to establish at New Delhi a large Central Research Institute. Harvey did much of the early planning for this important project, and later, in co-operation with the late Professor Starling, who was specially invited to India by the Government to advise on the subject. As Director he influenced medical research in India and advised Government on schemes for investigations. He attended various international conferences in different parts of the world as the representative of Government. He was also the Editor of the *Indian Journal of Medical Research*, to which he contributed many papers of much value. During the first world war he served as A.D.M.S. (San.) in Mesopotamia, 1916, till invalided to India. He was mentioned in dispatches for valuable services. In 1921 he was appointed a Companion of the Most Eminent Order of the Indian Empire (C.I.E.) in recognition of his outstanding work. Many enjoyed the kindly hospitality of his wife and himself at his

pleasant bungalow, beautifully situated in the Himalayas, at Kasauli, Punjab. In India he was a keen tennis player and much enjoyed a game. He retired from India in 1926.

After retiral he commenced the next phase of his career when he was appointed, on 1st October 1927, Histologist to the Research Laboratory of the Royal College of Physicians at Edinburgh. There he was again associated with his friend McKendrick, whom he succeeded as the Superintendent; later he became Director of Histo-pathological Research, a post which he held till his death. His work at the Laboratory was very fruitful and his skilled help in solving their problems was very highly appreciated by his colleagues and the profession generally, not only in Edinburgh, but far beyond. During this period he published important papers in this *Journal*. He was also the joint author of a monograph on "Debateable Tumours in Human and Animal Pathology." He had a wide and accurately recorded knowledge of original literature.

The irreparable loss to scientific medicine will, to some extent, be mitigated by the knowledge that he has left a large collection of material, meticulously arranged and card indexed. This will be a source of inspiration and a mine of accessible information for future research workers.

The College of Physicians of Edinburgh recognised his great services to them by awarding him: the Lister Fellowship, 1936; the Cullen Prize, 1946, "for the greatest benefit done to Practical Medicine"; and the Freeland Barbour Fellowship, 1947.

He was for many years a sectional editor of the *Bulletin of Tropical Diseases* and a regular contributor to it up to his death.

He became an F.R.S.E. and took a keen interest in the work of the Royal Society of Edinburgh, having served on its Council.

From what has been said above it will be evident that he led an exceptionally full and active life crowded with fulfilment to the very end. He was a very hard and systematic worker, and in the course of his career made important additions to our knowledge of scientific medicine.

We sympathise very sincerely with his wife, son and daughter in their great loss.

## FRANCIS SUTHERLAND

M.B., D.P.H.

SOME members of our profession are honoured for their personality or their discoveries; others for the impression they have made upon their patients: A third, and perhaps rarer type, seem to contribute something to the dignity of medicine itself, and to these last Francis Sutherland belonged. He was what is called "a character." Between 1917, when he qualified M.B. at Edinburgh, and August 1948, when he died in the same city, he spent most of his professional life in Scotland. He was an obvious and characteristic Highland Scot, yet his humanism was of a sort that is everywhere at home, and he was no "nationalist." After a brief and unusual assignment to investigate an obscure outbreak of typhus which had occurred in the island of Raasay off Skye, Francis Sutherland became a Medical Officer of Health for the Outer Isles, the first whole-time man to hold this post. His bailiwick included Harris, Skye, North and South Uist, Barra and some smaller and even less accessible islands; anyone who knows them in summer would envy

a man his work; but to sail between the Kyle of Lochalsh and Lochboisdale in January storms and then travel exposed to rain, peat smoke and island tracks, and moreover to carry on such a life for ten years—those are experiences requiring fortitude even in a man whose temperament really belonged to the open air. But Sutherland was not by nature such a man: though he enjoyed travel, he also loved meditation, talk, books and culture. He liked, moreover, to do his work with the utmost perfection of detail, and it was an irony of the public health organisation of these insular places that he had no clerk, no telephone, and no office. He was, in fact, his own secretary, and his typewriter set up in the hotel bedroom served him for a routine official correspondence of a style never heard of in the Hebrides either before or since. His epistolary manner was a model of official distinction and clearness of phrase. He always had the honour to be one's obedient servant, and no sanitary law or regulation ever escaped quotation. With such a paradoxical standard of perfection, he waded through the crude routine of island hygiene, examined school children, inspected nuisances, looked for contacts, surveyed sewage and lavatories. And after he had battled long with the fatalism of his Celtic patients and the inertia of an officialdom less gracious than himself, he would write up his findings in language not inappropriate to a Royal Commission. Yet Francis Sutherland had a strong sense of humour about himself and was the first to see that this distinction achieved in his protocols caused little but a vacuum. The Medical Officer of Health wrote the report, but the nuisance remained. This disproportion between diagnosis and achievement he realised fully, but he would have said, and he was correct, that until a high standard of official routine can be secured, there is no hope of good results in the public health of isolated places. Any hint that his efforts were futile, and that a more "practical" but less laborious approach would save time, would bring to his face a puzzled incredulity, and he would deliver a solemn but kindly rebuke.

Travellers in a highland hotel encountered at the fireside a red-haired, courteous person with a deep voice, ready with mimicry of Scottish ministers and queer tales of highland doctors. There was one magnificent series, almost a saga, about the fabulous Reverend MacDonald of Shildaig whose thought in Gaelic and speech in English had grotesque results. Sutherland told these stories with old-fashioned formality, and was prepared to argue over his whisky until morning if he had a worthy opponent for his dialectics.

After some ten years of this peripatetic hygiene, Sutherland obtained a more stationary appointment as Deputy Medical Officer of Health for Ross-shire, and for the first time was able to open his home with his own door key. His thoughts began to turn in the direction of psychiatry. Surely a surprising departure for a highland medical officer of health! But his father, Dr John F. Sutherland, had been an official of the Scottish Lunacy Board, and now his son decided to follow him into the same branch of medicine. With considerable persistence and ingenuity Francis Sutherland negotiated for the purchase of a large house on the River Thames at Staines and obtained a licence to treat patients under the Lunacy Acts. His new headquarters had belonged to the great cricketer, Prince Ranji Singhi of Jammagar, and Sutherland converted it into a private mental clinic, and here for a time he gave to his patients the same conscientious care that he had formerly devoted to island crofters. When some official demurred that the presence of a river so near at hand would prove a temptation to melancholic patients, Sutherland replied conclusively:

"Then I will set up an impassable barrier between the house and the water." He did and made a success of this establishment.

But the inward call of Scotland was insistent, and now a hereditary voice reinforced it. His father's old post, that of Deputy Commissioner in Lunacy, became vacant, and Francis Sutherland obtained it. For the next twelve years, he was able to combine his love for travel with his new interest in psychiatry as seen from an unusual administrative point of view, and now from the Butt of Lewis to the Neuk of Fife, from Muckle Flugga to the Mull of Kintyre, his journeys wound through Scotland. His patients were "boarded-out" cases under the Lunacy and Mental Deficiency Acts over whom the Board of Control exercises supervision. Sutherland was the ideal man to ensure that these unfortunates were humanely and kindly looked after. This form of domiciliary care for the mentally unfit he rated very highly, and he was scrupulous that the patient should have the most suitable guardian and the best possible surroundings. Until he had extracted every scrap of information which concerned each patient's welfare, his pertinacious mind and inexorable notebook were not to be satisfied. Many a doctor would have found this dull routine and would have slurred over the details. But to Sutherland this work was as fascinating as the most intricate laboratory work is to another man. It seemed that nature had been shaping him to be the perfect official visitor which this work required, and until we have better methods for dealing with mental disease and defect, such men as he will be needed.

His untimely death from cerebral hæmorrhage reflects the strain of those years of incessant movement, and that strictness with himself which compelled him to bring all his work to a meticulous standard.

Apart from reading, his real hobby was foreign travel. But here he had his own methods. Francis Sutherland was no superficial tourist. With Mrs Sutherland, he would read up in advance the country of his choice and learn some of its language. Then he would compel scenery, museums, food, and inhabitants to yield up the maximum of value in experience for which his careful schedule had prepared him. In this assiduous fashion he travelled over Europe to the North Cape, through France, Spain and Portugal, and he planned further journeys to Italy and Greece in a future retirement which he was not fated to enjoy.

Books and such travel experiences were more to Francis Sutherland than contemporary people. A colleague said he talked as Smollett wrote. Sutherland's taste in literature was austere. He believed that nothing good had been written since Robert Louis Stevenson, and Winwood Read and Lecky were often quoted. Such standards would have made him priggish but for that sense of humour which allowed him to laugh over the absurdities of everyday life, and made him guess that he himself was acting a part, that of the Victorian professional man. His polite idiosyncracies were observed quizzically by his outward personality, that broad, bluff, red-haired modern, dressed in plus fours, a cap and bow tie, who carried a stick, and always introduced himself into a patient's house with a stiff bow and a grave salute. That is the Francis Sutherland who lives in my memory.

HARLEY WILLIAMS.

## NOTES

At a Quarterly Meeting of the College held on 2nd November, with Dr W. D. D. Small, C.B.E., President, in the Chair, the following were elected to the Fellowship:—Graham A. H. Gumley, M.B. EDIN. (Dunfermline), S. Thiambiah, M.C., M.R.C.P. EDIN. (Vepery, Madras), Ernest Bulmer, C.B.E., M.D. EDIN. (Birmingham), John D. Ross, M.B. EDIN. (Kingskettle), Arthur W. Branwood, M.D. EDIN. (Edinburgh), Henry J. S. Matthew, M.B. EDIN. (Edinburgh).

The Diploma of Membership was conferred upon the following:—Leonard M. Comissiong, M.B. EDIN. (Grenada, B.W.I.), Esme G. L. Mark, M.D. EDIN. (Macclesfield), George A. Rail, M.B. CAPE TOWN (East London), Thomas G. Wilson, M.B. EDIN. (Berwick-upon-Tweed), Harold C. Falcke, M.B. RAND. (Verooniging), Israel Kessel, M.B. RAND. (Johannesburg), Walter R. Lang, M.B. N.Z. (Auckland, N.Z.), Colin C. Foote, M.B. N.Z. (Westport, N.Z.), Solly Lopis, M.D. RAND. (Johannesburg), Wilfrid A. B. Campbell, M.D. BELF. (Belfast), John W. Nelson, L.R.C.P. LOND. (N. Rhodesia), Mark S. Fraser, M.B. EDIN. (Edinburgh), Anthony F. J. Maloney, M.B. EDIN. (Edinburgh), Edgar N. Moyes, M.B. EDIN. (Edinburgh), Joan E. Spicer, M.B. EDIN. (Edinburgh), John D. T. Steele, M.B. EDIN. (Portobello), Jagdish C. Mehta, M.D. LUCKNOW (Agra, India), Alexander T. Macqueen, M.B. EDIN. (Edinburgh), William M. M. Lyon, M.B. EDIN. (Edinburgh), Patrick B. Fox, M.B. N.Z. (London), James S. Robson, M.D. EDIN. (Edinburgh), Mary K. MacDonald, M.B. EDIN. (Edinburgh), John A. Loraine, M.B. EDIN. (Edinburgh), Wickramaratnyge A. Karunaratne, M.B. LOND. (Ceylon).

The Hill Pattison-Struthers Bursary in Clinical Medicine was awarded to David Bull, L.R.C.P. EDIN.

Hill Pattison-Struthers Bursaries in Anatomy and Physiology were awarded to Mohamed A. Abdulla and Iain I. M. MacGregor.

THE examinations of the Board of the Royal College of Physicians of Edinburgh, the Royal College of Surgeons of Edinburgh, and the Royal Faculty of Physicians and Surgeons of Glasgow have just concluded at Edinburgh. The following passed the Final Examinations, and were granted the diploma of Triple Qualification Board

L.R.C.P. EDIN., L.R.C.S. EDIN., L.R.F.P. AND S. GLASG. on 23rd November 1948 : David Smith Anderson, Richard Aubrey Atherton, George Joseph Bagley, Percy Maurice Brazil, Philip Freeman, John Herbert Gentles, Harry Gerber, Louis Harold Geronimus, Susan MacArthur Gillies, Thomas Edward Grant, Jeremiah Cromwell Obiekwe Iwenofu, Josef Jochowitz, Alexander Logan, Leslie Cecil Luck, Kenmure Edward Maitland Melville, Martin Metz, Anthony Walter Phipson Millard, Arthur Joseph Mone, William McIlwraith, Monica Bonner Macnamara, Eleanor Dorothy Margaret Pierce, David Pride, Robert Fergus Reid, Ellen Mali Rosenthal, David Simon, Philip Herbert Slade, Reginald Augustine Spalding, Helen Lightbody Steven, David Stewart, Joseph Alexis Turner, Robert Wilson, James Winning, John Samuel Wood, Milton John Zimmerman.

## NEW BOOKS

*The Medical Bookman and Historian.* Vol 2, No. 1. Edited by F. C. DALLER, M.D., M.R.C.P., and W. R. BETT, M.R.C.S., L.R.C.P. 48 pages monthly. London: Harvey and Blythe. 1948. Price 2s. per copy.

This new venture has been running for a year. The greater part of the journal is taken up by reviews of new medical books. Some of these are done at considerable length, others are relatively short. The historical part of the journal occupies the central pages, so that, presumably, they may eventually be separated from the rest. This number deals with "The influence of Medical Poets on English Poetry," "Some Thyroid Pioneers," and "The Chloroform Centenary Exhibition at Edinburgh." There is also a short article on "Medical Eponyms."

The standard of production is good, but from the point of view of the purchaser there is one grave fault—that ordinary advertisements are strewn indiscriminately throughout the text.

*The Kingdom of the Lost.* By J. A. HOWARD OGDON. Pp. 256. London: The Bodley Head. 1947. Price 10s. 6d. net.

The author, who suffered from schizophrenia, was a voluntary patient for one year and a certified inmate for two years. He walked off and hid himself for fourteen days and thereby decertified himself.

He describes his disorder from the patient's point of view, gives an account of living conditions in the institutions and of the people he met in them. He took up Yoga and claims that it enabled him to regain his mental balance.

The book is an interesting story and should help to a better understanding of the patient's point of view.

*Der Blutspender.* By WILLENEGGER and BOITEL. Pp. 197, with 48 illustrations. Basel: Benno Schwabe & Co. 1947. Gebunden Fr. 10.

After a brief but adequate historical review of blood transfusion this book deals with the organisation of services providing blood and plasma in various countries. The psychological aspect of donor recruitment is dealt with and the comparative cost of blood and plasma in different centres is of interest. This book will be of value to those concerned in the organisation of a blood transfusion service.

*The Occasion Fleeting.* By HUGH BARBER, M.D., F.R.C.P. Pp. viii+200. London: H. K. Lewis. 1947. Price 15s. net.

One who has enjoyed practising in and around hospital medical wards for more than forty years should know something about some things, but he cannot be sure that it is worth the telling. Dr Barber has ventured to offer some of his thoughts and experiences in the hope that they may be instructive or interesting. He writes of many aspects of his experience, of his student-days, and of his experiences as a consultant, under such headings as "Clinical Acumen," "The Spirit of the Family Doctor," "Alcohol in its Place," "Idle Words," and so forth. The book is full of sound observations and wise sayings that should be very helpful to the young man commencing his career and no less of interest to the elder practitioner.

*Genetics in relation to Clinical Medicine.* By F. A. E. CREW, M.D., D.SC., PH.D., F.R.C.P.E., F.R.S. Pp. xii+111, with 16 figures. Edinburgh: Oliver and Boyd. 1947. Price 10s. net.

Professor Crew has addressed himself primarily to the student of medicine. He recognises that in the overloaded state of the curriculum the undergraduate will

not be interested in the academic aspects of comparative genetics, as he is merely seeking to acquire a knowledge of things which promise to be immediately useful. In order to appeal to the student and make the subject attractive, Professor Crew lays emphasis on the special genetics of man, though adequate examples in this field are necessarily very limited.

The book offers an introduction to the subject and gives a good account of all the important facts and should form a sure foundation for further study.

*Progress in Gynaecology.* Edited by J. V. MEIGS, M.D. and S. H. STURGIS, M.D. Pp. xlv+552, with 72 illustrations. London: William Heinemann Ltd. Price 35s.

This volume of seventy papers, contributed by seventy-one North American gynaecologists, is published for the purpose of refreshing and bringing up to date medical men who have been out of touch with gynaecology during war service. This aim it will indeed fulfil but it has a wider appeal. Practising gynaecologists and endocrinologists, as well as graduates preparing for higher diplomas will find it collects together and summarises much of the most modern views and practice which have developed as the result of recent progress and research in all branches of gynaecology and the allied subjects. A large section of papers is devoted to endocrine researches and their relationship to the management of the functional disorders. These indicate there is still much to be elucidated. Most papers have a short bibliography appended.

Dealing with the growing edges of a subject it is helpful to have the present opinions of accredited experts on controversial points. This the editors have secured by asking each author to write on his or her "hobby" and many of the names are well known in the literature in connection with the subjects they have chosen to expound in this volume.

*Personal Mental Hygiene.* By DOM THOMAS V. MOORE. Pp. vii+331. London: Messrs William Henderson. 1947. Price 21s. net.

The author points out that it is not sufficient to attain mental health to deal only with emotional conflicts, but that there is a higher and more spiritual side which the psychiatrist would do well to cultivate. It is natural that the author should think in the above manner, because as priest as well as psychiatrist, he is well equipped to present his point of view. In general, the book is stimulating and thought-provoking, and a strong plea is entered for less individualism and selfishness and for greater charity. It may be that too much reliance is placed on intense exhortation and some of the suggestions made are altogether too sweeping, e.g. the rise in cerebral arteriosclerosis connected with the great increase in the problems of smoking.

*Pharmakologie.* By K. O. MOLLER. Basel: Benno Schwabe. 1947. Price 48 francs.

This large textbook of pharmacology by the Professor of Pharmacology in Copenhagen was first published in Danish about five years ago and there have already been three Danish editions. It has now been translated into German and published in Switzerland. It is a sound work in the classical tradition. The actions of practically all the drugs used in medicine are clearly and accurately set forth for the benefit of students and practitioners of medicine. Substances without therapeutic action are only included when they are of toxicological importance. The preparations available in the German and Swiss pharmacopoeias are briefly described with doses. Recent famous discoveries such as streptomycin, paludrine, thiouracil and DDT are fully discussed, together with various drugs used on the continent of Europe and little known here. There is a list of over 2000 references to original work and many other references to reviews. The book will no doubt be a standard source of information, but it is not very easy to read. It concentrates on the results of



pharmacology without much emphasis on the methods by which these results were obtained. It thus tends to present the subject as a mass of facts scarcely more interesting than the facts of anatomy.

*Mental Health.* By J. H. EWEN, F.R.C.P.E., D.P.M. Pp. 267. London: Edward Arnold & Co. 1947. Price 12s. 6d. net.

This short textbook incorporates a chapter on special treatments and their practical technique, by C. Friedman. Mental health is discussed in an orthodox manner and consists essentially of a descriptive account of the various mental states comprised under the terms psychoneuroses, psychoses, and mental deficiency. The preventive and social aspects are not sufficiently stressed or elaborated. There are a number of small typographical errors which will no doubt be corrected in any subsequent edition, *e.g.* Kraepelin's date was 1896 not 1869. The book, however, may be regarded as an accurate synopsis of psychological medicine, but is more adapted for the use of undergraduates and psychiatric social workers than for post-graduates.

*The Doctor and the Difficult Adult.* By WILLIAM MOODIE, M.D., F.R.C.P., D.P.M. Pp. 296. London: Cassell & Co. Ltd. 15s. net.

Moodie believes that psychiatry does not attract the normal intelligent student. "It is a vague and indefinite subject—time consuming—tedious—irritating to those who like to do jobs quickly." While the author takes this point of view yet he has many wise things to say, and is essentially conservative and wary in relation to recent developments. The book is rather a puzzling one as the author seems to be a little perplexed as to how best to present his material. Much of it is the ordinary descriptive psychiatry found in any textbook, and one would like to have had the benefit of Moodie's large experience in regard to the problems of the more normal, but yet difficult adult.

*Inter-Allied Conferences on War Medicine, 1942-45.* Edited by Maj.-Gen. Sir HENRY L. TIDY and J. M. B. KNUTSCHBACH. Pp. 531. London: Staples Press Ltd. 1947. Price 50s. net.

During the war large numbers of troops from various countries were stationed in Britain from time to time and it was natural that the medical officers should be brought together to exchange information and views. A series of conferences were held under the auspices of the Royal Society of Medicine, at which many valuable papers were read. No reports of the meetings were published at the time but they have now been brought together in this volume.

The papers cover a wide range of medical interest and are grouped together in various sections. Some deal with purely administrative matters; others are of general medical interest and describe advances in knowledge and practice. There are records of achievement and, not the least interesting, stories of personal experiences.

This valuable collection of papers should be of interest not only to those who were privileged to serve but also to those whose obligations compelled them to remain at home.

*Ethics, with Special Application to the Nursing Profession.* By JOSEPH B. MCALLISTER, S.S., PH.D. Pp. xii+442. London: W. B. Saunders Company. 1947. Price 14s. net.

The author points out that his book is an effort to satisfy a growing demand for an approach to ethics which stresses principles and attempts to give some understanding of the speculative basis behind the principles. Contemporary life is unmoral and there is a great need for the development of basic convictions about moral principles. Nurses have social responsibilities beyond the average, and they must be familiar with deeper reaches of moral conduct and be able to defend right conduct as a firmly held conviction.

The book is well written in simple language and contains a vast amount of common sense and opinions with which any right thinking person would readily agree.

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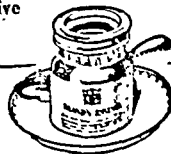
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## NEW EDITIONS

*Manual of Pharmacology and Its Application to Therapeutics and Toxicology*  
By T. SOLLMANN, M.D. Seventh Edition. Pp. ix+1132. London: W. B. Saunders Co. 1948. Price 57s. 6d.

Great changes have taken place in the use of drugs since the publication of the first edition of this book in 1917. Many preparations have lost their importance, though some of the older drugs are still unchallenged, but there has been a vast accession of new material.

A useful feature from the students' point of view and one which might well be considered by other authors, is the plan of printing the essential facts in large type and relegating to smaller type such data as would only be consulted when a special occasion arises.

This valuable work has advanced with the times and must still continue to hold its place as a leading textbook on the subject.

*Physical Methods of Treatment in Psychiatry.* By WILLIAM SARGANT, M.A., M.B. (CANTAB.), M.R.C.P., D.P.M., and ELIOT SLATER, M.A., M.D. (CANTAB.), M.R.C.P., D.P.M. Second Edition. Pp. xx+215. Edinburgh: E. & S. Livingstone Ltd. 1948. Price 10s. 6d. net.

This book has been added to and brought up to date. It is a very good, clear, and on the whole fair statement of the place physical methods have come to occupy in the treatment of a vast variety of psychiatric conditions. While chief prominence is given to insulin, convulsion therapy, and pre-frontal leucotomy yet other treatments as well are carefully considered. For instance the treatment of general paralysis with malaria and penicillin, and the treatment of the epileptics are all given in detail. The book, therefore, is a valuable one for both students and post-graduates.

*The Natural History of Disease.* By JOHN A. RYLE, M.A., M.D., F.R.C.P. Second Edition. Pp. 484. London: Oxford University Press. 1948. Price 22s. 6d. net.

The first edition of this book appeared in 1936 and had a gratifying reception. Professor Ryle now offers a new edition somewhat modified because of advances in treatment and containing some new material. His ideal is to regard the physician as a naturalist, for no amount of scientific training or technical ability can supply those qualities of naturalist and of humanist without which the good physician can never fully earn his title. Most of the articles in this book are concerned with disease in the individual, but the author as professor of social medicine has added a chapter on the natural history of rheumatic fever in the country. He claims that most of our textbooks need re-writing and his contributions suggest the lines along which changes should be made.

A stimulating book which merits the attention of all those who practise medicine.

*The Foot and Ankle.* By PHILIP LEWEN, M.D., F.A.C.S. Third Edition. Pp. 847, with 389 illustrations. London: Henry Kimpton. Price 55s. net.

The third edition of Lewen's textbook is considerably enlarged, as one would expect since the war has brought into prominence many new observations on the foot. Subjects which have been given additional emphasis are compound fractures, crushing wounds, and chemotherapy. In discussing treatment the author states that he has tried to tell the reader what to do, when to do it, and what not to do. If any criticism is suggested it is that there are no clear indications of how to do it. An attempt has been made to include all methods, as for example in the treatment

of club foot where twelve ways of curing the condition are described, even to a description of "decancellation" of the tarsal bones, here stated to be recommended by Curtis but really dating back to Ogston of Aberdeen and years ago realised to be an unwise procedure. It is equally difficult to know what is recommended in claw foot. The description of the logic and method of Lambrinudi is poor.

In spite of many obvious faults there is much to be said in favour of this book, especially if the reader has enough experience to choose the reasonable method from the number described.

It is very well reproduced and the diagrams and line drawings are beautifully done and most helpful.

*Communicable Diseases for Nurses.* By A. E. BOWER, A.B., M.S., M.D., F.A.C.P., and EDITH B. PILANT, R.N. Sixth Edition. Pp. xi+657, illustrated. London: W. B. Saunders Co. 1948. Price 20s.

This is an important member of a series of books specially written for the nursing profession. Several chapters are devoted to general matters such as immunity and infection and the care of communicable diseases in the home and in the community. Then follows a short account of each of the diseases with especial reference to the nursing problems which arise. The book covers a wide range of subjects including not only the common fevers, but the venereal diseases and such things as tuberculosis, influenza, poliomyelitis, tetanus and so forth.

The matter is well presented and the book should be most useful to those who possess a copy.

*The Essentials of Modern Surgery.* By R. M. HANDFIELD-JONES and A. E. PORRITT. Third Edition. Pp. xix+1256, with 644 illustrations. Edinburgh: E. & S. Livingstone Ltd. 1948. Price 50s. net.

The third edition of this popular textbook appears within ten years of its original production, a testimony to the quality and popularity of the work. The book has been completely revised and new chapters on chemotherapy and amputations have been introduced. The chapter on anæsthetics has been omitted. The revision has been carried out efficiently and while, as is inevitable in such a work contributed to by many authors, there is some inequality, the standard, taken all over, is very high.

The authors have adhered to their original plan of publishing the book in one volume, necessarily somewhat bulky, but the advantages of the plan are considerable.

The illustrations throughout are excellent and the paper, printing and general production of a very high standard.

*Essentials of Fevers.* By GERALD E. BREEN, M.D., B.CH., D.P.H., D.O.M.S. Second Edition. Pp. xi+351, with 24 illustrations. Edinburgh: E. & S. Livingstone Ltd. 1948. Price 15s.

This book gives a complete yet concise account of the common infectious diseases. To keep the volume abreast of recent advances in medicine new sections on typhus, glandular fever, undulant fever, encephalitis and food poisoning have been added, while the chapter on dysentery has been expanded and re-written.

The author, as his own artist, has attempted to give the student a realistic yet diagrammatic picture of the typical rashes seen in certain of the infectious fevers. These are reproduced as coloured plates. The book should prove a useful manual to both student and practitioner.

*Medicine—Essentials for Practitioners and Students.* By G. E. BEAUMONT, M.A., D.M. (OXON.), F.R.C.P., D.P.H. (LOND.). Fifth Edition. Pp. 831, with 71 illustrations. London: J. & A. Churchill Ltd. 1948. Price 30s. net.

In the six years that have elapsed since the publication of the fourth edition considerable advances have been made in medicine. This latest edition contains

a number of new articles on such subjects as infective hepatitis, homologous serum, erythroblastosis and thiouracil. With numerous further additions and alterations, it has, in fact, been brought completely up to date. The text is lucid and the illustrations are helpful to beginners.

In so far as it is possible to-day to compress medicine into 800 pages, the author has succeeded, but dogmatic statement necessarily takes the place of reasoned argument. For medical students and the general practitioner this book remains, as it has always set out to be, a most useful textbook.

*Diseases of the Nose, Throat, and Ear.* By I. SIMSON HALL, M.B., CH.B., F.R.C.P.E., F.R.C.S.E. Fourth Edition. Pp. 463, with 82 illustrations and 8 coloured plates. Edinburgh: E. & S. Livingstone Ltd. 1948. Price 15s. net.

The form of the book is the same as that of the previous edition, but the subject-matter has been brought fully up to date. In particular, the widespread application of penicillin has necessitated changes in the treatment of infective conditions, and a special section on penicillin has been added to the chapter on chemotherapy. The section on otosclerosis has been slightly expanded to include an assessment of the results of the fenestration operation. The book remains ideally suited to meet the needs of the student and the general practitioner, for whom it was originally written.

*Gardiner's Handbook of Skin Diseases.* Fifth Edition, edited by JOHN KINNEAR, O.B.E., T.D., M.D., M.R.C.P.ED., D.L. Pp. xiv+250, with 80 illustrations and 20 coloured plates. Edinburgh: E. & S. Livingstone Ltd. 1948. Price 15s.

An attractively produced handbook of dermatology which presents the essentials of the subject in a form calculated to appeal to both the senior student and the busy practitioner. A notable feature is the excellent quality of the coloured plates which are of definite diagnostic value. This textbook fulfils a real need in that it provides excellent material for students who have insufficient time to study more bulky volume and might otherwise tend to rely solely on lectures notes or clinical teaching and thus neglect a subject of great interest and importance to all practitioners.

## BOOKS RECEIVED

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- CORLETTE, C. E., M.D., CH.M., F.R.A.C.S. A Surgeon's Guide to Local Anæsthesia. (John Wright & Sons Ltd., Bristol) 35s.
- CURRIE, J. R., M.A. (OXON.), M.D., LL.D. (GLAS.), D.P.H. (BIRM.), F.R.C.P. (EDIN.), and MEARNS, A. G., M.D., B.Sc. (Public Health), D.P.H. (GLAS.), F.R.S. (EDIN.). Hygiene. Third Edition (E. & S. Livingstone Ltd., Edinburgh) 35s. net

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# Edinburgh Medical Journal

November 1948

## VALEDICTORY ADDRESS

By Dr W. F. T. HAULTAIN, *O.B.E., M.C., F.R.C.P.E.*  
*F.R.C.S.E., F.R.C.O.G.*

IN this my Valedictory Address to you it is my first duty to thank the Fellows of the Society for the support they have given me during the past two years and for their kindness and forbearance for any deficiencies I have shown as the occupant of this Chair. Especially have I to thank the Council for their great help and in particular the Senior Secretary, Dr MacGregor, who has been the live wire in all the arrangements that were made for your edification and entertainment. Resuscitation is never easy, especially after a period of eight years when our thoughts and lives have been occupied with much more serious and in some cases more dangerous activities. It is therefore most gratifying to be able to tell you that during the last two years forty-five new Fellows have been elected and the Society has had what I consider to be a most successful Session, a matter to which I will refer later in more detail. It would be unusual, however, for two years to pass without a Society such as this suffering grievous losses and during this period one Honorary and six Ordinary Fellows have passed from our midst, and to these I would desire now to pay tribute.

Professor Daniel Dougal of Manchester, who died on 4th June 1948, was one of our most recent Honorary Fellows; he will be missed not only by us as a Society but by the whole obstetrical world, as his name was famous. He was a true Scot, even though he spent most of his life in Manchester, and was an able successor to two famous predecessors, who had also Scottish connections, namely Archibald Donald, who was Edinburgh born and educated, and Fothergill, who qualified in this city—all names that will always be remembered in gynaecological history. Dougal was perhaps best known for his work on endometriosis, the clinical features of which Donald had commented upon many years previously, and we in this Society were fortunate to have heard Professor Dougal speak on this subject in 1938. Besides his professional attainments Dougal was a most delightful man, and I can speak from personal knowledge as I worked with him at St Mary's Hospital in 1921 when I was resident house surgeon to Professors Donald and Fothergill, and Dougal was the junior assistant to the Hospital. At that time, having just returned from distinguished

Read to the Edinburgh Obstetrical Society, 1948.



service with the army, Dougal was not as busy as he afterwards became and spent a great deal of his time devising gadgets many of which were tried out at St Mary's. The chief one at that time was a mackintosh covering for the skin of the abdomen which was attached to an oval cane which had to be manœuvred through the abdominal incision; with anæsthetics not so good as they are now and the apparatus being in its raw state, this procedure was sometimes very difficult and it would take often as long as fifteen minutes to accomplish. As this usually occurred late in the afternoon at the end of a list started by Fothergill, when Dougal started his work primed with lunch, but not so the resident staff, it can be imagined how we viewed this particular gadget, but Dougal's personality was such that his popularity with the resident staff did not suffer. Great affection was accorded to him by all, juniors, contemporaries and patients alike.

Dr Charles Mowbray Pearson was one of our oldest Fellows, being elected to the Society in 1902. He was one of the grand old school of general practitioners, who took a great interest in midwifery and though he never read any paper to the Society, he took part in the discussions from time to time. We are glad that the family tradition is being carried on and welcome his daughter as a member of the present Council.

Three other general practitioners from more outlying areas have also died: Dr A. L. S. Tuke, whose name was a household word in Dunfermline for many years, in fact as far as medicine was concerned Dunfermline was Tuke. Though elected to this Society in 1901, he was not a very active member as his bent was in favour of general surgery rather than midwifery. Dr Marshall of Peebles and Dr Angus Macdonald of Kelso were both very well known in the Borders; both were keenly interested in midwifery with the result that they attended most meetings of the Society even when the weather was so inclement that the Edinburgh Fellows were fearful regarding their journeys home especially as Soutra had to be encountered by the latter. They frequently took part in discussions and their sage remarks regarding the general practitioners' standpoint will be greatly missed. Dr Marshall was elected a Fellow in 1912 and Dr Macdonald, elected in 1926, served as a member of Council from 1933-35.

Dr Eneas Kenneth Mackenzie of Tain, another famous general practitioner and a name to conjure with in the North of Scotland, died in March 1947. He was elected to the Society the same day as Dr Macdonald. There is little doubt that midwifery was the part of general practice in which Dr Mackenzie was most interested, and had his financial position on qualification allowed it he would have devoted his life to this one speciality; it must therefore have been most satisfying to himself to know that he was looked upon by his fellow practitioners as an authority in this branch of medicine. He did not write any papers for our Society, but he had been asked to represent the general practitioners' standpoint in the discussion held

in December 1946 on the role of the general practitioner in future midwifery practice; he was, however, unfortunately unable to accept the invitation owing to his state of health. You will remember that instead he wrote a long letter to the Society, which was read at the meeting and which put forward his ideas in his usual forceful manner. He took a vivid part in the discussion on the "Scottish Departmental Report on Maternal Mortality and Morbidity" in December 1935. Dr Mackenzie wrote many letters to the medical journals from time to time protesting about interference in general practitioner midwifery; these letters often contained a tirade against specialists in general and any authority accorded to them by the Department of Health, but we who knew him understood that these letters were written by a man who by wont and practice was a real specialist in the subject and could not realise that there were very few practitioners who possessed his knowledge or had attained his prowess or experience in the practice of midwifery. In reality he appreciated the individual specialist and enjoyed the many conversations he had with them, conversations which were of mutual benefit to himself and to them.

Just recently we have lost one of the oldest of our Specialist Fellows in the person of Edward Fow Fisher, who joined the Society in 1921 and was on the Council from 1923-25. After a distinguished career in the navy during the 1914-18 war, during which period he was based for a time at Rosyth, Fisher found the attractions of Edinburgh so great that he gave up a busy and lucrative practice near London to become assistant to the late Dr Haig Ferguson. He had obtained his English F.R.C.S. several years previously and lost no time in acquiring the Membership of the Royal College of Physicians here. He was at one time gynaecologist to the Deaconess Hospital and Richmond Street Dispensary and latterly was a member of the Board of Management of the former Hospital. Fisher was welcomed by his obstetrical colleagues in this city and made many good friends outside as well as inside the profession amongst whom he was deservedly popular. Personally I would like to pay tribute to him as a man and also for his strenuous service as Medical Officer to the 4th Battalion Home Guard almost from its inception at a time in his life when he had gained the right to a happy and quiet retirement. He will be greatly missed by his large number of friends.

Lastly we deplore the untimely end of one of our youngest Fellows, Dr R. C. Wood, who died after a four days' illness from infantile paralysis contracted in his practice. "Bertie," as he was known to all of us, had taken the trouble to try to become acquainted with all branches of medicine before he settled down to general practice, and in order to do this had held resident posts in medicine, surgery, midwifery and gynaecology and pædiatrics; he was probably most interested in his work amongst the children and was becoming justly popular as a family doctor in the true sense. After a long and arduous war service he had just settled down in Edinburgh, had been elected

an assistant physician to Leith Hospital and was busy acquiring an excellent practice when he was stricken. Popular with everyone he is sorely missed and Edinburgh medicine is all the poorer by his untimely end.

The work of the Society during my two years of office has been varied, one of the main objects being to make the Society acceptable not only to the specialist but also to the general practitioner who practises and is interested in midwifery. That being so, no fewer than six papers of special interest to the general practitioner as well as to the specialist were contributed and it was satisfying to hear the practitioners taking their share in the discussions which followed. Five of our younger Fellows contributed interesting papers on original work, a fact which shows that the Edinburgh school is by no means dormant and augurs well for the future. We have also had the good fortune to have been able to arrange several special nights, when the programme was out of the ordinary due either to the special eminence of the lecturer or to the presence of the Glasgow Obstetrical Society as our guests, who took their full share in the evening's proceedings. The last Meeting of the Session contained both these features, for not only were we able to welcome one of our latest Honorary Fellows, Dr A. D. Campbell of Montreal, but also the Glasgow Obstetrical Society, to a meeting held in the Hall of the Royal College of Surgeons, after which we all dined together in the Library; a most fitting site for such an important meeting. To my mind it is most satisfactory that these combined meetings with the Glasgow Society inaugurated by Professor Hendry just before the war have not been allowed to lapse, as they tend to broaden our outlook, and the dinners held after the meetings lead to greater fraternity and friendship between the two Societies and their respective Fellows.

Dr Douglas Guthrie provided variation by reading an historical paper on "Peter Camper," which was most appreciated.

This year we welcomed another guest in Mr Charles Read, who combined with Professor McWhirter in opening a discussion on "The Treatment of Cancer of the Cervix," a subject that was well discussed and thrashed out before the evening ended to the benefit of all the large number who attended.

During the previous year we had the pleasure of welcoming one of our own Fellows as our principal lecturer for the Session, in Professor Chassar Moir, who read a paper on the "Treatment of Urinary Incontinence," a subject which has come again markedly into the limelight during the last years and to which Professor Moir has played a most significant part. The papers on widely varied subjects, which Professor Moir has read before this Society from his resident days until now have always been most original and this was no exception; it was most appreciated not only by the Fellows of the Society but also by a number of surgeons who had been invited to attend the meeting and take part in the discussion.



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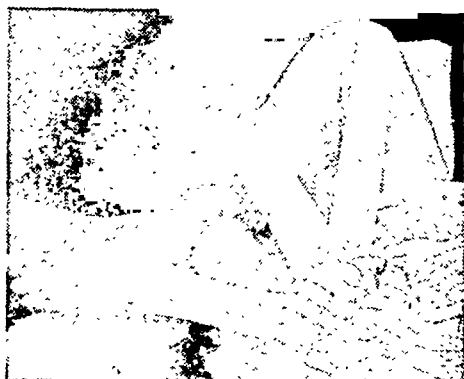


Fig. 1 (Above)

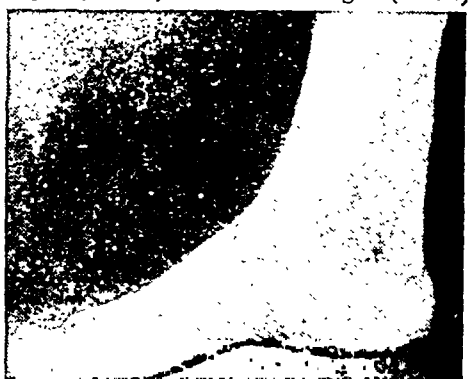


Fig. 2 (Below)

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Lastly, who among us who had the fortune to be present two years ago to-night will ever forget the most masterly and whimsical paper which the retiring President, Professor Johnstone, rendered as his Valedictory Address. It will long be referred to and read when many of the other papers will I fear be forgotten.

As it would be far beyond my powers in this my Valedictory Address to try to emulate the feats of rhetoric and oratory of my predecessor, when I considered a subject which would be worthy of your attention, I decided it would be wise to avoid anything ethereal, but literally to come down to earth and give you some solid facts about the maternity service under the National Health Services Act which we are now expected to carry out.

It has been my fortune, good or bad, as one may view it, to have been on several committees associated with the production of the new National Health Services Act and to be at present on the Regional Hospital Board of the South-East Region. I have therefore had the opportunity of studying the Act in some detail and have been able to co-ordinate from numerous authoritative circulars and instruments those facts which interest us as obstetricians or as general practitioners practising midwifery, which many present may not have been able to do. I thought therefore that for the time remaining this evening that you might appreciate a résumé of the working of the Act, as I see it, in so far as it relates to our branch of medicine. It must, however, be remembered that details are not entirely completed and in the light of experience there may be changes, but I hope that I will be able to put before you the position midwifery holds in the South-Eastern Region of Scotland at the moment.

It is a great misfortune that the maternity services have not been placed under one authoritative body and I would like to endorse fully the view of the Royal College of Obstetricians and Gynæcologists, which was so ably put forward by our present President, Sir William Gilliatt in a letter to *The Times* on 9th July, in which he stated: "... The Royal College of Obstetricians and Gynæcologists has from time to time stated its views on the maternity services to be provided under the National Health Service Act. . . . We reiterate our conviction that the care of the pregnant woman, whether at home, at the clinic or in hospital, is a responsibility which cannot be discharged with the maximum safety to the two lives at stake if it is shared between different administrative bodies. The importance of full co-ordination in reducing maternal and infant mortality is so great that the duty of providing a co-ordinated scheme for all aspects of maternity work must be placed unequivocally on one authority at regional board level. . . . The college has always advocated that it is desirable to have a list of practitioners who have had experience of midwifery after qualification to be called in for midwives' emergencies under the Act. . . . It appears now that any practitioner can undertake maternity work under the Act. He may not necessarily be present at the

confinement but will be called upon in an emergency. The principle which the college has always recommended will be discarded if such a practitioner does not possess the experience mentioned above." This union, which we take to be essential for the practice of midwifery under the Act has not, alas, been achieved and in Scotland midwifery is under three separate administrative controls, which must co-ordinate satisfactorily if any useful Service is to be produced. Thus in regard to domiciliary midwifery the *general practitioners* act under the Executive Councils, the *midwives and local authority ante-natal clinics* are under the supervision of the Local Authorities, and the *Specialist and Hospital Services, including the ante-natal clinics in hospital premises*, are under the control of the Regional Hospital Board. The work of these three bodies in relation to midwifery must be discussed separately in the first instance and at the same time reference made to matters for which the closest liaison and co-operation is required.

#### THE GENERAL PRACTITIONER SERVICE UNDER LOCAL EXECUTIVE COUNCILS

Every woman in the United Kingdom is entitled to the services of a doctor and a midwife, should she so desire, to supervise her confinement, and all practitioners in Scotland who desire to undertake midwifery can do so provided they enrol on the midwifery panel with the Executive Council. Every enrolled practitioner will receive a fee of seven guineas for each domiciliary case for which he must give the same attention as he did under the Maternity Services Act for Scotland, 1937; namely, for normal cases he has to undertake three ante-natal examinations, one as early as possible during pregnancy and certainly before the fourth month, the second about the thirty-sixth week and the third at the thirty-eighth week; he also has to pay a puerperal visit within twelve hours of delivery and undertake a post-natal examination between the fourth and sixth week in the puerperium; he does not, however, need to attend the labour if he considers that all is expected to be normal, but has to be on call should the midwife require his services. The doctor is responsible for the necessary urine analysis and the estimation of the blood pressure but the urinalysis is often delegated to the midwife who reports at once if any abnormality is present. If the case is not normal then the practitioner will have to undertake as many examinations and visits as he considers necessary. A practitioner not wishing to go on the midwifery panel can undertake a midwifery case should he desire to do so but will only receive five guineas for the same services; it is, however, considered that such practitioners will be very few as anyone can put his name on the panel and yet not be compelled to take cases he does not wish to attend. Any practitioner may take private cases, but only from outside his panel. If the practitioner is not, on the

midwifery panel and does not desire to do any midwifery then he will assist his patients to make the necessary arrangements for their confinements. In England where the arrangements are different, suitably qualified practitioners will be placed on a midwifery panel and will be available for summons by midwives when required, as well as attending their own cases; such practitioners will receive seven guineas a case, whereas those not recognised can still attend their own cases, but will only receive five guineas for each case. The question of the "suitably qualified" practitioner is a very vexed one and has been the cause of much wordy warfare, but as I directed attention to this subject in my Presidential Address a year ago there is no need for further expansion now.

A certain proportion of the beds in nearly all the maternity hospitals in the South-East Region will be available for the general practitioner to look after his own confinements, the number varying in the different hospitals according to the local circumstances. These practitioners will be recompensed as for domiciliary cases, except where they are on the staff of the hospital (*e.g.* Cottage Hospitals) when they will only receive a fee of three and a half guineas for ante-natal and one guinea for post-natal care; they will, however, be paid in addition the proportion of £25 per bed per annum which is due them from the staff pool.\* If the patient makes arrangements to go into a nursing home for her confinement then the practitioner will still consider the case as far as he is concerned a domiciliary one and he will receive the usual fee of seven guineas. Should a specialist be called in by the practitioner for such a case in a nursing home, it would appear that as far as he is concerned also the case can be considered to be domiciliary and he will be recompensed according to the domiciliary scales. Likewise if any specialist is called in to a nursing home for consultation to a patient, who is not under his care there, this also comes under the heading of a domiciliary consultation. Practitioners attending their cases in hospitals will have to conform to the usual hospital routine and will be expected to report any abnormality to the specialist staff, asking for its advice and help, as the specialist must retain the ultimate responsibility; all such hospital patients will be asked to pay at least one ante-natal visit to the hospital, preferably about the thirty-sixth week; if this was not done then the hospital would not be able to accept the necessary responsibility.

At any time during the pregnancy or labour the practitioner can call on the services of a specialist as part of the Hospital and Specialist Service either by sending the patient to hospital if she is able to travel or by asking for a domiciliary visit if she is not able to do so. If the

\* This has now been rescinded and practitioners will be recompensed as for domiciliary cases, whether they are on the Staff of the hospital or not. He will, however, be remunerated by the Regional Hospital Board for the confinement and for any ante- or post-natal care rendered at the hospital. The average number of beds used for such confinements will not be included in the assessment of beds occupied at the rate of £25 a year per bed.



patient has to be admitted to hospital before labour and has her confinement in hospital then the practitioner will only receive the ante- and post-natal fees, but should she be in labour at the time of admission then he will receive the full fee.

If a practitioner is called in by a midwife for a patient who has not engaged him for her confinement his fee will be four and a half guineas, but this will include puerperal attendance as well and a post-natal examination. For a single attendance at labour the fee will be two and a half guineas, but if the perineum has to be sutured or the baby resuscitated three guineas will be paid. A fee of four guineas will be paid for attendance for an abortion or threatened abortion or ante-partum hæmorrhage, but this will include visits for fourteen days after. If a second practitioner is called in to administer an anæsthetic for a confinement he will receive a fee of £1, 15s.

### THE LOCAL AUTHORITY

The Local Authority is responsible for providing the midwife who will generally be chosen by the patient, and for the provision of ante-natal and post-natal clinics as well as those for infant welfare. An independent midwife engaged will receive £4 per case, but in many areas the local authorities are themselves providing the services of midwives by appointing to their staffs whole-time salaried midwives, who are remunerated on an agreed national scale.

It is to be hoped that ante-natal and post-natal clinics in the larger towns and districts will be staffed, as has been done previously in Edinburgh, by the younger specialists of the maternity hospital staffs, who will act as ante-natal officers for the ordinary routine work, but will be able to give specialist advice to those patients attending the clinic who require such advice or treatment and also to any patients referred to the clinics for such advice by their own doctors. The remuneration of the specialist should therefore be shared by the Local Authority and the Regional Board as the specialist is carrying out duties for each. These ante-natal clinics should be affiliated to one of the maternity hospitals in the town or district and the medical officer if possible, should be on the staff of such a hospital so that the responsibility can be transferred from the clinic to the hospital and any mistakes can be duly commented upon and practical experience gained thereby. In the smaller towns such arrangements might not be possible and it would be of great advantage both to the patient and doctor if the practitioner were allowed the use of a clinic for the thorough examination of his patients.

The presence of a health visitor at all ante-natal clinics would be most beneficial as she would be able to give patients advice on such domestic and personal matters regarding which the doctor has not the time nor the necessary knowledge to discuss.

In order to give continuity between the ante-natal clinics and the

maternity hospital it is essential that the patient should have a copy of her ante-natal record which on admission she will take to hospital with her. This might either be an abbreviated record with every 1 record,

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a) Post-Sp. - also Sp. <  
b) Degree: changes in respiration - diffusion of gases <

Residual air >

Vital Capacity < (half)

V.L. of dead Sp. >

Minute Vol. & Resp. Rate >

Depth of Resp. <

Inte-pl. pres. > (= atur) bld. return < Inc. Venous Pres.

Symptoms: Irritations over

Shortness of breath on exertion (in adv. & some) -  
moderate cyanosis → ~~Swelling~~ (as in Cong. HT) in  
winters: persistent bronch. - In adv. d., both in winter & summer

→ Cardiac decompensation - orthopnea, edema legs  
Intercess. of Pres. → Death

Signs: lungs: shallow, rapid breathing

\* All these sums are assessed on a 1939 basis and therefore approximately 20 per cent. will be added in each case to give the present-day amounts.

members each from the Royal College of Physicians, London, and the Royal College of Surgeons, England, two each from the Royal College of Obstetricians and Gynæcologists and the three Scottish Royal Corporations, and one each from the Medical Research Council, the Universities and the lay public. There will be no reward for seniority as such and it will be quite possible for a junior to receive more remuneration than his senior. This recommendation of the Spens Committee does not seem to have found favour with the majority of specialists, for though the younger specialist is treated most favourably, little or no provision is made for experience, which all will agree is a very important attribute in every speciality. The system of meriting awards is probably meant to deal with this to some extent but many specialists with ripe experience will doubtless be overlooked and the awards may be given to specialists of the "back-room" variety, who have had little experience in the humdrum arduous routine of the hospital specialists' work. The fair choice of recipients for these awards will be almost impossible on account of the great difficulties surrounding the task, and will I fear give rise to much heart-burning and jealousy from which in Scotland, at any rate, in the past we have been singularly free. You will appreciate that there must be a limit to the number of persons accepted as of full specialist status—in other words, with public money involved, there must be a specialist establishment for the hospital region. The attainment of full specialist status will depend on a person's experience and qualifications, and there being a suitable vacancy available.

Full-time is defined as eleven half days and specialists doing part-time work will be paid proportionately to his age and status to the number of half days he devotes to hospital work plus one quarter of  $x/11$  where  $x$  is the number of half days worked. Extra remuneration will be given for teaching. All specialist appointments to hospitals will in future have to be advertised and the applications considered by an Appointments Committee; this Committee will consist of two members from the Regional Board, two from the Hospital Board of Management concerned, two specialists taken from a panel of specialists, which has been formed for such a purpose and who for each individual appointment will probably be specialists in the branch of medicine or surgery for which the appointment is being made, and either six or two university representatives depending upon whether the appointment involves major teaching duties or not. This Committee will draw up a short list in order of preference for the Hospital Board of Management concerned, who will advise the appointment for the concurrence by the Regional Board, who are the deciding authority. This machinery is only invoked for appointments above the grade of registrar or resident medical or surgical officer, as these more junior appointments which are for the trainee class of potential specialists, will be made on the advice of the Medical Committees by the Hospital Boards of Management concerned, who

will also appoint the more junior resident staff. The potential specialists will be divided into three classes: (1) those who have been qualified for not less than one year, at a fixed salary of £600; (2) those who have been qualified for not less than two years and who will normally hold their posts for two years, the salary being £700 for the first year and £800 the next, and (3) those who have been qualified for not less than four years who will hold their posts for normally three years, the salary being £900 rising by two annual increments of £100 to £1100 per annum. If the post is held for a further year then the salary will rise to £1200, at which figure it remains.\*

*Hospital Services.*—Maternity hospitals will in the majority of instances have to cater for both normal and emergency midwifery and a proportion of beds will have to be kept available for emergency cases. They will also have to make accommodation for ante-natal patients, the proportion of beds varying in different hospitals, but as a general rule at least 30 per cent. should be available for ante-natal cases and from 10 to 15 per cent. for emergencies. As cases of incomplete abortion are a source of danger in maternity hospitals and as they occupy beds in gynæcological wards urgently required for gynæcological cases, it is essential that in a city such as Edinburgh separate arrangements should be made for their treatment; all such cases requiring hospital treatment should be accommodated in a ward delegated for this purpose alone. This would be in the best interests of the patients and would also permit of scientific investigations to be carried out regarding the causation of abortion by obstetricians, embryologists, sociologists, etc., from which valuable information might accrue. In the other areas this plan should be carried out also if at all possible.

Booking for patients who desire to be confined in hospital should be effected by a letter from the patient's doctor asking for her admission and sending her with the note to the hospital of choice. If that hospital has been fully booked for the date required then enquiries will be made by that hospital, from an admission bureau if available, as to what other hospitals have vacant beds; the patient then makes her choice and she is sent to that hospital to make the necessary arrangements and her doctor written to regarding what has taken place. Not all women who apply can be admitted to hospital for their confinements, therefore patients will have to be selected either for medical or social reasons and all needful cases will be admitted; if there is no definite reason for hospital delivery, then if the practitioner and patient agree, these patients can be treated as district cases by the hospital staff. A doctor's letter requesting admission for his patients was rarely sent in the past and most women came to the maternity hospitals to make arrangements on their own, which was unsatisfactory to all concerned;

\* All these sums are assessed on a 1939 basis and therefore approximately 20 per cent. will be added in each case to give the present-day amounts.

now, however, as all patients have a doctor there is no reason why the admissions to the maternity department of a hospital should be any different to the other departments, where a doctor's letter has always been required. The receipt of a letter from the doctor besides telling the hospital that the doctor desires the patient's admission will help the doctor to keep an efficient record of his patient as he will then be notified (1) if she can be admitted, (2) if not, where she can be admitted, or if admission is impossible anywhere, the suggestion that she may be delivered on the district, (3) on discharge from hospital he will be notified, information being given regarding her pregnancy, confinement and puerperium and the condition of the child, and (4) after the post-natal examination he will again be informed that all is well or of any abnormalities that were present. Should the practitioner refer his patient to a hospital to book for her confinement then the ante-natal care will be carried out by that hospital and the practitioner can only undertake the responsibility of her ante-natal care by arrangement with and on behalf of the hospital with access to a specialist from the hospital where necessary.

Maternity hospitals, as in the past, will play an integral part in the training of midwives and some will afford teaching facilities for students as well in practical midwifery. In the larger hospitals midwives will be able to train for both Part I and Part II of the C.M.B. Examination, but the hospitals in the outlying districts will be unable to train nurses for Part I, as they will not have the teaching staff available. These hospitals must, however, be staffed with nurses and it is considered that in a number of cases they will be able to undertake the training of pupil midwives for Part II examination. The pupils will in such cases be posted for two to three months, depending on the number of cases available, to suitably qualified midwives in the surrounding townships to do their necessary district work and will spend the remainder of the six months training in the hospital. By such means a large field of as yet untapped district cases will be made available, which will make a most important contribution in contending with the present scarcity of cases in the larger maternity hospital districts; at the same time the smaller hospitals will be staffed efficiently and satisfactorily. These pupils will have to attend their key hospital for lectures, but as these only number six at the most for those training for Part II, this could be easily effected and the training for gas and air anæsthesia could be augmented at the smaller hospitals for those who had not been able to get sufficient cases during their Part I training. This scheme would not only help the hospitals to obtain staff, but would help the district midwives in their work and the pupil would live in the same atmosphere as she will practise in when qualified.

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the hospital. If regular visits are required weekly or more often the fares are paid for patients coming from 5 miles or more. If a companion is absolutely necessary then the companion's fare will be paid as well as that of the patient. From the economical standpoint as well as in the patient's best interests, it will be essential that out-patient departments especially for gynæcological cases are established in the larger centres in the area, and that these are serviced by specialists in contradistinction to the present-day practice of practically all gynæcological out-patients requiring to come to Edinburgh from Fife, East Lothian, Berwickshire or the Borders. Likewise ante-natal clinics might be established in smaller townships such as Leven, Lochgelly, St Andrews, etc., in affiliation with the maternity hospitals rather than allowing the patients to travel to the main centre clinic at Kirkcaldy or Dunfermline. This has already been tried out in a small way at Bangour, and judging from the increasing attendance of patients both ante-natal and gynæcological, would seem to be appreciated by both patient and doctor. In the course of time this would give a welcome and necessary relief to the Royal Infirmary gynæcological out-patient department. Should a patient go into labour and require admission to hospital during the night and no transport is available then an ambulance may be called upon. All ambulances are now under the ægis of the Regional Hospital Board with the exception of a few private ambulances, and most of these also are under contract to the Board, the main exceptions being some special ambulances which are attached to coal mines.

*Maternity Benefit.*—There is a maternity grant of £4 for each baby independent of whether only the husband is insured, or both husband and wife. If the patient has been working and has contributed for a half of the previous fifty-two weeks and for at least forty-five of these weeks has she been at work or been registered as unemployed or sick, she will receive 36s. a week for thirteen weeks beginning six weeks before the expected date. If she has not been working or contributing then she will receive 20s. a week for the four weeks following the confinement.

It will be seen that the practice of midwifery under the National Health Services is not exactly simple to understand and many facts have to be collected and collated. It will be still harder to work the scheme satisfactorily and all will have to give of their best to try and make it effective. The success of the scheme will depend largely on the liaison between its three integral parts, the Executive Councils, the Local Authorities and the Regional Hospital Boards, and success will only be attained if these liaisons are carried out harmoniously and indulgently by all the parties concerned. To do this a great deal will depend on the individuals concerned—the practitioner, the specialist, the medical officer of health, the midwife and the patient herself.

Though probably no one here to-night is in full agreement with



the scheme in its entirety, it is our duty to do our best and to make the scheme work out by playing our *individual* parts as well as each of us can, for only by doing so can our patients' interests best be served and our British posterity be made improved.

And now it only remains for me to hand over the reins of office to my friend and colleague Dr D. C. Fahmy. All here know Dr Fahmy well and no words of commendation on my part are required. I would, however, remind you how much the Society owes Dr Fahmy for his services in the past, as he was Secretary for nine years from 1926-35 and has been a Vice-President since 1939. He therefore is very well versed in all matters connected with the Society and has always had its welfare very much at heart. It is with the greatest pleasure and the utmost confidence that I now ask Dr Fahmy to occupy the Presidential Chair.

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*Maternity Benefit.*—There is a maternity grant of £2 for each baby independent of whether only the husband is insured, or both husband and wife. If the patient has been working and has contributed for a half of the previous fifty-two weeks and for at least forty of these weeks has she been at work or been registered as unemployed or sick, she will receive 36s. a week for thirteen weeks beginning six weeks before the expected date. If she has not been working or contributing then she will receive 20s. a week for the four weeks following the confinement.

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And now it only remains for me to hand over the reins of office to my friend and colleague Dr E. C. Fahmy. All here know Dr Fahmy well and no words of commendation on my part are required. I would, however, remind you how much the Society owes Dr Fahmy for his services in the past, as he was Secretary for nine years from 1926-35 and has been a Vice-President since 1939. He therefore is very well versed in all matters connected with the Society and has always had its welfare very much at heart. It is with the greatest pleasure and the utmost confidence that I now ask Dr Fahmy to occupy the Presidential Chair.

# SCLEROSING ANGIOMA—A NON-MELANOTIC PIGMENTED TUMOUR OF THE SKIN

By E. K. DAWSON, M.A., M.D.

Grantee of the Cancer Control Organisation of Edinburgh and  
South-East Scotland

*(From the Research Laboratory of the Royal College of Physicians, Edinburgh)*

WITH newer methods of therapy now in use for certain types of tumour growth, accurate diagnosis, based not only on knowledge of the structure of the lesion but also on its tissue of genesis and its probable life history, has become even more necessary, if the results of different methods of treatment are to be assessed on a comparable basis. In some tumour conditions, the clinical picture is sufficiently diagnostic to justify the therapeutic procedure adopted without histological confirmation, but whenever possible, examination of the diseased tissue should be made, to uphold the claim to successful treatment.

The study of pigmented tumours of the skin suggests that their clinical picture is frequently misleading. Histological examination is therefore usually necessary, both to establish the nature of the pigmentation and to support or refute a diagnosis of possible malignancy. Prognosis in malignant melanotic tumours is, in general, so unfavourable that pigmentation which is brownish or black and suggestive of extension is rightly regarded with uneasiness. The "black tumours of the skin" discussed by Roussy, Huguenin and Queyn (1935) included three different types, the "true malignant melanomas" of nævus cell origin, the "tattooed epitheliomas," both basal and squamous cell and the "angiofibromas" or sclerosing angiomas. In their experience, clinical distinction is usually impossible. If the lesion prove a melanoma, the therapeutic implications may be serious. The colour of any particular skin tumour, however, may be due to the presence of pigments other than melanin, even when the clinical appearance suggests melanoma. Moreover, the type and degree of coloration in cutaneous growths depends not only on the nature of the pigment, whether melanin, hæmosiderin or some lipochrome, but also on its amount, the level of its deposit in the cutis and the condition of the overlying epidermis. Another important factor in diagnosis may be the vascularity or actual hæmorrhage, if the growth is in an area exposed to trauma.

Melanoma, hæmangioma and "xanthoma," uncomplicated by hæmorrhage or ulceration, may raise little clinical doubt regarding their nature, though, as regards the melanoma, even this statement needs qualification. As M. C. Tod (1946) points out, "if the tumour is red or pink, it may be very disconcerting because it is biopsied (before irradiation) under the impression that it is squamous or basal

cell carcinoma (or angioma ?) but is reported as a melanoma. Such a biopsy is dangerous but inevitable." In her table of survival figures for malignant melanoma (*loc. cit.*), which suggests that the darker the colour, the more malignant the condition, pigmentation ranged from black, through dark and light brown, blue and purple to red and pink. The essential question in diagnosis and prognosis in the melanotic group is whether the growth is benign or malignant, but in non-melanotic skin tumours, hæmorrhage, with the deposit and possibly slow removal of hæmosiderin, may produce a pigmented picture which also presents a diagnostic problem.

Through the generous co-operation of several colleagues, an opportunity has been given me to study a small group of pigmented skin tumours, all of which were of doubtful import. Their colouring ranged from brownish-pink to black; some appeared melanotic and were considered possibly or definitely malignant; others suggested fibromatous or neurofibromatous lesions. A description of their structure and a brief discussion of their relationships to other tumour types seems justified in view of their misleading appearance and also because of the variety of names under which similar growths are reported in the literature. Follow-up notes of the cases studied are unfortunately wanting, in most cases, partly due to the movement of patients during and after the last war, but where available, were unexpectedly favourable.

The following case reports, in summary, include most of the group studied.

1. *Female act. 66.*—"Clinically, melanoma on leg; history of injury to the area four years previously. Lesion treated by irradiation (mould) without effect. Recent excision." Sections show a characteristic, early stage, sclerosing capillary angioma of lenticular shape, the "tumeur en pastille" (Fig. 1,  $\times 1\frac{1}{2}$ ); hæmorrhage and much granular pigment, proved hæmosiderin; hæmangiomatic structure, with cell whorls, "pools" of pigmented cells and early fibrosis, as in Figs. 4, 6 and 23; vasoformative pattern brought out by reticulin stain (Fig. 2,  $\times 180$ ); ulceration. No evidence of melanoma or malignancy. Patient was treated for cancer of cervix seven years ago and now, two months after removal of angioma, not well and having "giddy turns"; a hard area in scar on leg.

2. *Female act. 70.*—"Ulcer on leg; appears a melanoma." Sections show ulceration, with some superficial infection; abundant pigment deposit (Fig. 3,  $\times 90$ ), proved hæmosiderin; some capillary angiomatous structure, with moderately cellular intercapillary tissue (Fig. 4,  $\times 220$ ); in other parts, a diffuse cellularity with more pigment, some hyalinisation and no pattern (Fig. 5,  $\times 400$ ); sparse groups of foam cells. No evidence of melanoma.

3. "Large pedunculated tumour of the skin, clinically suggesting melanoma." Sections show tissue of capillary angiomatous structure (Fig. 6,  $\times 100$ ), intra- and extracellular pigment, proved hæmosiderin (Figs. 7,  $\times 200$ , 8 and 9,  $\times 500$ ) and fibrosis with some hyalinisation. No ulceration, no evidence of melanoma.

4. *Female act. 34.*—"Ellipsoid, firm, blue-black, intra-cutaneous tumour of forearm, clinically malignant melanoma; duration three to four years.

slow enlargement one year ; no previous treatment, no palpable lymph nodes." History of trauma, as "began as an infected mosquito bite with later injury by a dog's claw." Sections show abundant hæmosiderin deposit reaching to flattened epidermis (Fig. 10,  $\times 90$ ) ; dilated vessels forming "pools" filled with pigmented cells and red blood cells and separated by plump spindle cell tissue (Fig. 11,  $\times 250$ ) ; deeper parts show tissue of cellular angiomatous pattern (Fig. 12,  $\times 250$ ) with very sparse pigment. No ulceration ; no evidence of melanoma.

5. *Adult female*.—"Angiomatous-looking tumour of leg, with rapid growth during last few weeks." Sections show capillary angiomatous structure (Fig. 13,  $\times 270$ ) in a cellular background with much hæmosiderin deposit ; active fibrosis ; some channels (lymph ?) containing free cells and pigment (Fig. 14, at  $\times$  ;  $\times 270$ ). No ulceration or malignancy.

6. *Young male*.—"Large hæmorrhagic growth over scapula ; nature of tumour clinically doubtful." Sections show sparsely pigmented, poorly differentiated, vasoformative whorled tissue with some telangiectasis (Fig. 16,  $\times 140$ ) ; diffusely cellular areas with abundant, coarsely granular pigment deposit, proved hæmosiderin (Fig. 17,  $\times 140$ ) ; scattered groups of foam cells with positive Scharlach R reaction, in a cellular background (Fig. 18,  $\times 140$ ) ; much hæmorrhage. Periphery shows rounded macrophages, heavily pigmented with hæmosiderin (*cf.* Fig. 15). A very rare mitotic figure but no evidence of malignant growth.

7. *Male aet.* 29.—"Pigmented tumour of right forearm, bleeding ; sent for irradiation as 'incompletely excised melanoma likely to recur' ; no note of pre-existing mole." Sections show diffusely cellular tissue forming, to the naked eye, a lenticular growth, "tumeur en pastille," in the dermis (*cf.* Fig. 1) ; hæmorrhage with pigment, proved hæmosiderin ; some multinucleated cell formations containing pigment granules and lysing red blood cells ; scattered foam cells. No melanomatous structure (Fig. 19,  $\times 80$ ). No irradiation given. Later history, soundly healed scar, no palpable lymph nodes ; patient dismissed after observation, well, two years and three months after tumour first observed.

8. *Male aet.* 17½.—Clinically, "malignant melanoma of scalp." Sections show angiomatous structure, partly cavernous, partly capillary ; the cavernous channels almost filled with hyperchromatic, endothelial cells mixed with red blood cells and separated by capillary areas (Figs. 20,  $\times 80$  ; 21,  $\times 400$ ). Hæmorrhage but no hæmosiderin deposit in areas examined. Later note, patient has a bald patch, but dismissed from observation, well, a year after excision of growth.

9. *Male aet.* 38.—"Pigmented, raised tumour on thigh, present for 'some time' ; positive iron reaction ; diagnosed histologically as sclerosing angioma." Sections show cords of hyperplastic endothelium with little lumen formation ; scattered pigmented cell aggregates ; intra- and extracellular pigment and a fibrillar and collagenous stroma. No ulceration ; no malignancy. A recent case.

10. *Male aet.* 35.—"Small, slightly pigmented, thickened area in the skin and subcutaneous tissue, now very hard, but present for years as a softish lump ; increased in size and became harder a few months ago ; other small, similar lumps in skin of limbs, about a dozen." Sections show superficial resemblance to neurofibroma, with slight palisading of nuclei, but structure, on close analysis, shows fibrosis round numerous compressed capillaries, the

aggregated endothelial nuclei lying parallel and forming, in places, pseudo-giant cells; a tissue pattern of small whorls in some areas; much hæmorrhage and considerable pigment deposit, mainly extracellular. These features point to a sclerosing angioma rather than to neurofibroma.

11. *Female aet.* 47.—“Tumour from skin of deltoid region, pigmented; recurred after incomplete removal six years previously. More rapid growth last two years.” Sections show, as in case 10, structure suggestive superficially of neurofibroma, with apparent palisading of nuclei, but close study reveals many collapsed and compressed capillaries with parallel-lying endothelial nuclei; some cavernous vaso-dilatation; sparse intercapillary cellularity and much fibrosis; no pigment or foam cells in plane examined; no suggestion of malignancy.

12. *Child aet.* 6.—“Patch of injected, roughened and thickened skin on forearm and another similar patch on buttock; tuberculide? or neurofibroma?” Sections from the forearm lesion show a nodular fibroblastic tissue, extending from mid zone of dermis into the subcutaneous fat, the nodules containing numerous compressed capillaries grouped round small arterioles or venules; sparse hæmorrhage, no obvious pigment; diffuse capillary overgrowth also in the fatty tissue. Considered a sclerosing capillary angioma of the lobular type, not neurofibroma, but this stage of fibrosis rather non-diagnostic. No suggestion of sarcoid.

13. *Female aet.* 38.—“Tumour on shoulder, raised, oval, 1 cm. diameter, firm, pink, no symptoms; duration sixteen years; slow growth at first, none for several years. Clinical diagnosis ‘subepidermal nodular fibrosis.’” Sections show an ill-defined cellular area in the dermis, sparing the papillary zone (Fig. 22,  $\times 50$ ); varied structure with capillary angiomatous tissue in small whorls and little lumen appearance (Fig. 23,  $\times 140$ ), similar to Fig. 16; other areas show more advanced intercapillary fibrosis (Fig. 24,  $\times 150$ ). No pigment or foam cells.

14. *Baby*.—“Pigmented nævus on foot.” Sections show a capillary angioma with dilated vessels evenly filled with blood; much intra- and extracellular hæmosiderin deposit between the vessels and in the stroma beyond the angiomatous area. No evidence of active fibrosis in the small piece examined, but supporting tissue hyaline, with few nuclei. No foam cells; no nævus cells.

Other illustrative lesions were also studied. They included other sclerosing angiomas, with no clinical data, three “blue nævi,” melanotic tumours of the epidermal layers (“hard nævi” or “tattooed epitheliomas”), two Kaposi’s sarcomas and a cerebral hæmangioma (Lindau’s disease?). Three of these are summarised.

15. *Male aet.* 18.—“Pigmented tumour of eyelid, clinically malignant melanoma; excised, with extensive dissection of cervical lymph nodes; sent for irradiation. No sections of lymph node tissue available but primary site and scar in neck healthy and no irradiation given; patient well, with no sign of tumour, three years and one month after excision.” Sections from eyelid tissue show abundant pigment in the dermis, both extracellular and in spindle cells, mainly perivascular (Fig. 25,  $\times 80$ ). Nature of pigment not ascertained but its fine granulation and even distribution in the cells point to melanin, not hæmosiderin. No angiomatous structure. These

features favour a diagnosis of "blue nævus," a benign melanotic lesion of the dermis.

16. *Girl aet. 14.*—"Very black lesion on arm; noticed seven years ago, at vaccination; now is itchy and perhaps has grown a little; iron reaction negative; blue nævus?" Sections show structure similar to eyelid tissue (case 15), with abundant, pigmented spindle cells, most numerous round hair shafts; no angiomatous appearance. Confirms diagnosis of blue nævus. Well, no recurrence, fifteen months later.

17. *Male aet. 22.*—"Very vascular cerebral tumour, blocking the foramen of Magendie and causing hydrocephalus." Section shows numerous anastomosing capillaries lined by swollen endothelium, in a matrix of foam cells of varying size and somewhat indefinite outline (Fig. 27); no obvious hæmosiderin deposit in the small piece of biopsy tissue available for examination. No clinical data regarding cyst formation or angiomatous growth elsewhere (retina, etc.), but this tissue illustrates Lindau's original description (1926) of swollen, phagocytic, fat-laden endothelial cells in angiomatosis of the central nervous system, retina, etc.

Although most of the cases suggested a melanotic tumour, clinically, histological study, in all but the blue nævi and the melanotic warts ("hard moles" or "tattooed epitheliomas"), revealed a capillary angiomatous structure, varying from a cellular, poorly vasoformative tissue to the quiescent sclerosing form. Blood pigment deposit was confirmed in most cases; foam cells, though present in some degree in the majority, were much less abundant than in many reported cases, only the cerebral tumour showing the degree of lipid ingestion seen in advanced xanthomatous change. The clinical histories, though rather meagre, are characteristic and instructive.

## DESCRIPTION

In the following text, the lesion is described as "tumour" in the somewhat loose application of the term to angiomas, whether regarded as neoplasia, hyperplasia or malformation. Cholesterol and lipid cover the various fat and lipid substances in the blood.

No uniform or characteristic picture of the sclerosing angioma is obtained by the study of a series of cases. This, however, is not surprising, for two independently variable factors are operative, a tumour or malformation of great morphological variety and an involution process which may come to examination at any stage. A composite picture, however, emerges.

*Clinically*, even when the microscopical pictures are similar, appearances may vary greatly and are rarely diagnostic. There may be a history of a congenital nævus or of a long-standing lesion with slow growth for some years, then quiescence, followed by later increase in size or pigmentation (*cf.* cases 4, 5, 10). The tumours may be multiple but are usually solitary. Geschickter and Keasbey (1935), in a series of 570 hæmangiomas recorded at Johns Hopkins Hospital, found multiple tumours in only 5 per cent. of surgical and

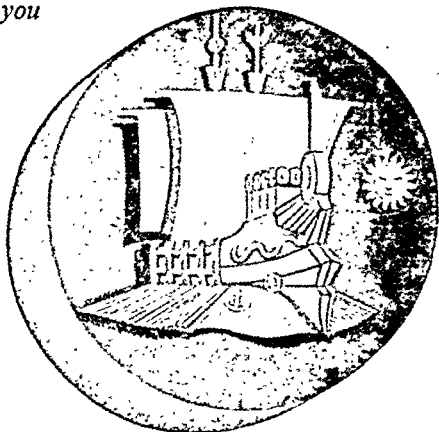


autopsy cases. The tumour is painless, usually small and mobile on the deeper tissues; its colour varies from black to shades of violet, purplish-brown, red, dark and light brown, pink and yellow. It may be soft at one stage and harden later. In advanced stages of fibrosis, the lesion may show only a pink or white depressed scar, but the excised tumour is usually a projecting growth, hard or soft, sometimes with a brown or reddened base. Some have been described as falling off (Best, 1926; Sézary and Horowitz, 1933). The clinical features are probably determined by the initial type and extent of the angioma as well as by the stage of sclerosis. This latter feature is usually well-established at the time of excision, as the condition has been frequently diagnosed as fibroma—Unna's fibroma simplex—and given such names as "fibrome en pastille" (Sézary and Lévy-Coblenz, 1933), dermatofibroma (Traub and Monasch, 1932; Willbrandt, 1932; Stecker and Robinson, 1941) or nodular subepidermal fibrosis (Michelson, 1933; Sutton and Sutton, 1939). Sutton (1942) describes this "fibroma," with fixation of blood pigment in its tissues, as pseudo-melanomatous. Most of the lesions have been observed on the limbs, shoulders and buttocks, that is, in areas most liable to trauma but some have been described on the face and indeed, in almost any site. The majority are removed before ulceration has occurred but when increase in size and intensified pigmentation have made them suspect. Their varied appearance is indicated by the clinical difficulty in deciding whether the lesion is melanoma, blue naevus, angioma, neurofibroma, solitary cutaneous leiomyoma, "xanthoma" or a post-inflammatory condition ("granuloma pyogenicum"). Some reported cases were also considered epidermoid carcinomas or "angiosarcomas"; many were described simply as "skin sarcoma," especially if multiple, in children.

*Histologically*, as indicated in the tissues illustrated here, the picture also varies within a wide range, from very cellular or almost purely capillary to a fibrous or xanthomatous type and it is difficult to describe any appearance as typical. Except when large and hæmorrhagic, as in case 6, the growth usually shows a circumscribed, though ill-defined lenticular outline in the dermis, forming a "tumeur en pastille" (Fig. 1), which may spare the papillary zone (Fig. 22). The overlying epidermis may be unaffected or thinned or hypertrophic, sometimes with excessive melanin pigmentation (Woringer and Kviatkowski, 1932), or, rarely, ulcerated. I have observed no skin appendages in the affected area; nerves were occasionally found but only at the periphery. A few larger vessels, normal or dilated, may be present in the tumour area but the tumour *grundlage* is essentially capillary. The cellular picture is often complex and difficult to analyse and has been frequently misinterpreted. In general, there is some recognisable capillary vasoformative character, which, at an early stage, is more or less differentiated in pattern, with small hæmorrhages from fragile blood vessels of immature tumour type. Later, one finds

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cords or groups of aligned proliferated endothelium, small cell-whorls and anastomosing, compressed-looking capillaries, with or without lumen. The cell-whorls, giving a "floral," "fan" or "étoilé" appearance, are almost diagnostic of angiomatous tissue. With progressive sclerosis, the intercapillary fibrous tissue increases, often with a patchy hyaline change, or a diffusely cellular, rather amorphous picture is produced, with isolated or grouped cells, endothelial, histiocytic and fibroblastic, difficult to identify or distinguish. This somewhat polymorphic, cellular appearance and especially "the rather confusing spindle cells" (Garrett, 1924), has sometimes led to a histological diagnosis of malignancy (Dupont, 1933, 1939) but this is not supported by the structure or by the later history. Hæmorrhage and hæmosiderin deposit may be sparse or abundant. Hæmosiderin is seen as coarse, brownish-orange, intra- and extracellular granules, in H-E sections, or as fine particles giving a faintly bluish tinge, by the iron test, to histiocytes in various stages of enlargement. Bernstein (1939) described foam cells in his case as "histiocytes before saturation with hæmosiderin," giving a positive prussian blue staining. These cells, when large and rounded or oval, form one type of the phagocytic cell which has given the tumour one of its commonest names, "histiocytoma." They may be scattered through the tumour tissue (*cf.* Figs. 3-13) or at a later fibrosing stage, be more numerous at the periphery, forming a partial "halo" round the growth, as seen in Fig. 15, from a section stained for hæmosiderin. Many of the lesions also show histiocytes with ingested blood cholesterol and these form the more characteristic foam cell, of lipid-containing, xanthomatous type. In the few recorded cases where the lipid content of the circulating blood was ascertained, it was within normal limits, so the focal xanthomatous condition had no obvious connection with a systemic (metabolic) disturbance. Illustrated reports (*e.g.* by Gross and Wolbach, 1943) and my own observations show that hæmosiderin and lipid material are sometimes present together in the same phagocytic cell, the cytoplasm showing coarse pigment granules standing out against a finely granular, foamy background, in cells which give a positive staining reaction to both iron and fat. Diss (1938) also describes this. But many recorded cases show, at the time of examination, a predominantly or exclusively lipid foam cell formation and to such a degree that much of the tumour is replaced by xanthomatous tissue. The lesion may, however, fibrose and disappear without passing through an obvious pigmented or xanthomatous phase, as was observed by McDonagh (1912) and shown in some of the cases described here. Multinuclear giant cells are found in some cases, formed by "the coalescence of nests of endothelial cells, isolated by sclerosis" (Gross and Wolbach, *loc. cit.*), but careful study at high magnification suggests that many of these are produced by vascular endothelium fusing round lysing blood cells, in a collapsed or thrombosed capillary. None of the tissues examined showed cholesterol crystal clefts surrounded by

ordinary foreign-body giant cells. Some tissues also show dilated spaces or "pools," lined by endothelium and containing compact masses of pigmented cells mixed with red blood cells (*cf.* Fig. 11) and variously interpreted, in the literature, as blood or lymph channels. These "alveolar cavities" are accepted by Dobkévitich and Marques (1939), Bernstein (1939) and others as evidence of hæmangiomatic character; Ulrich (1921), who also illustrates this feature, said these spaces reminded him of lung alveoli filled with heavily-pigmented heart-failure cells (siderophores). At a late stage of sclerosis, the tissue becomes largely fibrous, sometimes with scattered, peripheral, hæmosiderin- or lipid-laden histiocytes. This fibrous stage, with little or no remaining angiomatous element, resembles an inactive fibroma, or a non-diagnostic fibrosis which has replaced a nævus-cell tumour or a neurofibroma (*cf.* case 12).

### DIAGNOSIS

The history and the clinical appearance of pigmented skin lesions may be so misleading that most observers emphasise the necessity of complete removal, with histological examination for diagnosis, before any more radical treatment is undertaken as in case 15. Ten of the 28 cases of "dermatofibroma" studied by Stecker and Robinson (1941) were considered malignant before examination; they also note that the condition may be clinically confused with squamous carcinoma, rodent ulcer or sarcoma, as well as with melanoma, neurofibroma, etc. But even under the microscope, the complex and variable picture may be difficult of interpretation, if unfamiliar. Recognition of the angiomatous structure depends mainly on the histological features already described—some capillary formation is usually present, even though obscured by pigment and fibrosis—but also on remembering that both hæmosiderin and melanin produce pigmented tissue, clinically and microscopically evident. Macroscopic examination of the cut surface after excision may provide little help, if pigmentation is brownish or black and abundant. Bloodgood (1924) described the brownish-red and yellow or grey and yellow mottled appearance of "xanthoma" as characteristic and distinguishing it from hæmorrhagic sarcoma or malignant melanoma, but he noted that all benign tumours with this peculiar mottled colouring are not necessarily similar in structure. Diagnosis of a cellular fibrohæmangioma in frozen sections needs, in his opinion, much experience.

The histological pattern of the tissue usually excludes *melanoma* without difficulty, but proof of the nature of the pigment, obtained most conveniently by the iron reaction, is important additional evidence, with the caution, given by Smith (1924), that pigment granules of hæmatogenous origin may give no iron reaction in cases of old hæmorrhage. Also, ulcerated melanomas may show hæmorrhage with blood pigment in phagocytes in the tumour area. Omission to distinguish between melanin and hæmosiderin in the tumour cells

may undermine a claim to successful therapy of a lesion presumed melanotic and malignant, especially where microscopical examination shows a diffusely cellular picture with little or no vasoformative pattern and much pigment (*cf.* Fig. 17), with a non-diagnostic history of a naevus of long duration, possibly from birth, with recent increase in size and colour. It is instructive to note that, in many reported cases and in some of my series, even when the histological picture proved to be angiomatous and presented no pathological diagnostic difficulty, initial therapy was based on the clinical likelihood of melanoma, possibly or probably malignant. Exposure to trauma and hæmorrhage into the tumour tissue, notoriously associated with the activation of a quiescent mole, may have been responsible. The distinction between hæmosiderin and melanin in routine H-E sections is not always as easy as is sometimes suggested (Becker, 1934; Smith, *loc. cit.*). Stout, who has done much work on blood vessel tumours (1943, 1944), emphasises and illustrates the additional help in diagnosis given by the silver reticulin stain, which brings out the distinctive pattern of the delicate fibrous supporting framework round the vascular tubes of the hæmangiomatous tissue (*cf.* Fig. 2).

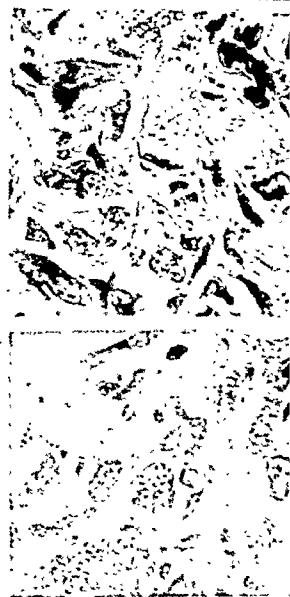
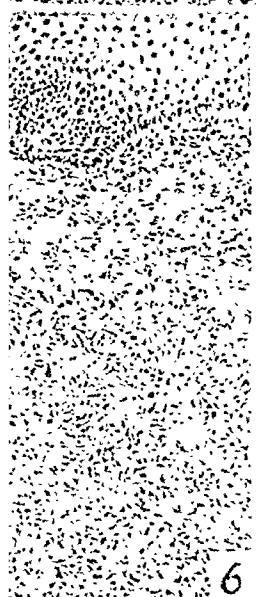
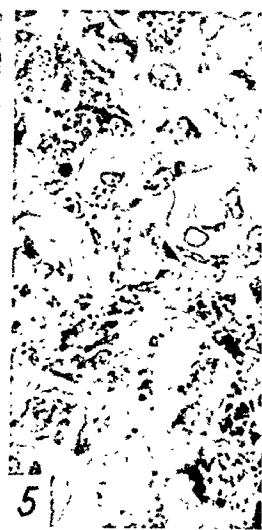
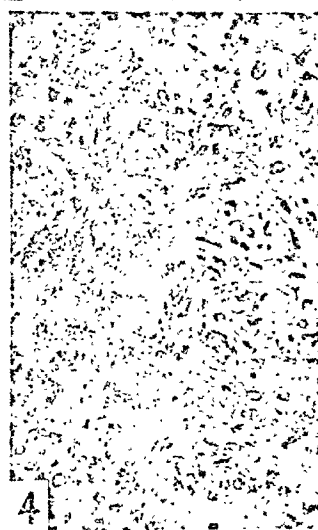
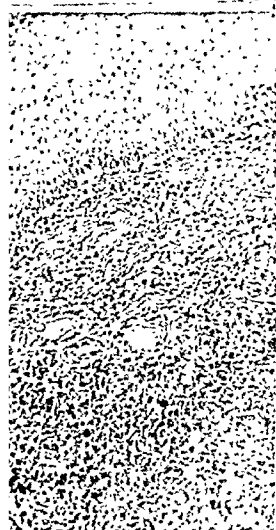
If the test for hæmosiderin is negative, the condition may be a *blue naevus*, a rare melanotic lesion which may also gradually fibrose with age and shows little if any tendency to true tumour growth (Montgomery and Kahler, 1939; Willis, 1948a), though it may show extension, sometimes at puberty, as in case 16. In some cases of my series (Nos. 10, 11, 12), collapsed capillaries with parallel-lying, compressed endothelial nuclei suggested the palisading of a *neurilemmoma* or a *neurofibroma*, which may also be solitary and show skin pigmentation and some spontaneous fibrosis. Stout (1935) also describes hæmorrhages with old phagocytosed blood as well as lipid-containing foam cells, in nerve sheath tumours. High-power analysis of the microscopical picture and, if necessary, silver staining, leave little diagnostic doubt. Ewing considered that many, if not indeed the majority of cutaneous fibromas were really neurofibromas; my own study of an admittedly small number suggests that some, at least, were initially angiomatous rather than neurofibromatous. Both tissues may, however, be found together and with naevus cells, in some pigmented moles, which we may regard as complex malformations involving all the structural elements of the skin area, epidermal and mesodermal.

A *cutaneous leiomyoma*, when small, solitary, superficial, painless and covered by pigmented skin of brownish, reddish or bluish colour (Stout, 1937), might be a clinical problem, but raises little histological difficulty, for though the muscular tumour tissue, in many cases, suggests a foundation on the media of abnormal blood vessels (Stout, 1937; Lendrum, 1947), the sclerosing angioma is essentially of capillary structure. Sutton and Sutton (1939) note that the clinical manifestations of *cutaneous Hodgkin's lymphadenoma* "may puzzle

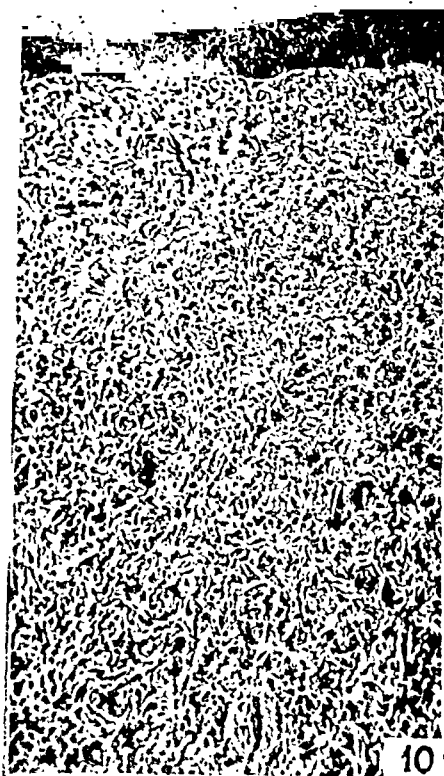
the most astute observer," for it may produce a pigmented, solitary, ulcerated lesion. The few cases of "*granuloma pyogenicum*" which I have had opportunity to examine all suggested an ulcerated, infected capillary angioma, though the term, as used by the dermatologists, implies or includes a post-traumatic, hypertrophic area of infected and hæmorrhagic granulation tissue. Garrett (loc. cit.), in a study of Bloodgood's collection of xanthomatous tumours, described a group of "*granulation tissue tumours*," almost if not quite identical with his fibro-hæmangiomas or sclerosing angiomas. Clinically, the relations of these three conditions, sclerosing angioma, "granulation tissue tumour" and "*granuloma pyogenicum*," are very ill-defined. If the angioma is ulcerated, it may also be difficult to distinguish it microscopically from a hypertrophic, infected "*granuloma*," unless the lesion is removed *in toto* and the deeper, non-infected tissue examined. A history of a pre-existing nævus, possibly of long duration, before ulceration and an angiomatous tissue structure below and lateral to the ulcerated area, would point to angioma. MacKee and Cipollaro (1936) note that small early nodules of *Kaposi's sarcoma* (cf. Fig. 26) often resemble angioma or granuloma pyogenicum and Rattner and Neuhauser (1940) describe the proliferation of blood vessels and hæmosiderin deposit in early, multiple Kaposi lesions, but these become confluent and the condition, when examined, usually shows the vascular lesions at a more advanced stage, with nodular plaques and a tendency to symmetrical distribution.

As already mentioned, no cutaneous case in my small series showed the extensive xanthomatous change which, in many recorded instances, led to a diagnosis of "histiocytoma" or "xanthoma" and masked the essential, underlying angiomatous structure. This xanthomatous appearance, even when the lesion is small and apparently solitary, opens up the wide question of systemic disturbances which may manifest themselves by lipid deposits in the skin and other tissues. A consideration of these is beyond the scope of this study, which was suggested by the diagnostic difficulty raised by some cutaneous pigmented tumours clinically suggestive of melanoma, but one or two aspects of the question are mentioned under discussion.

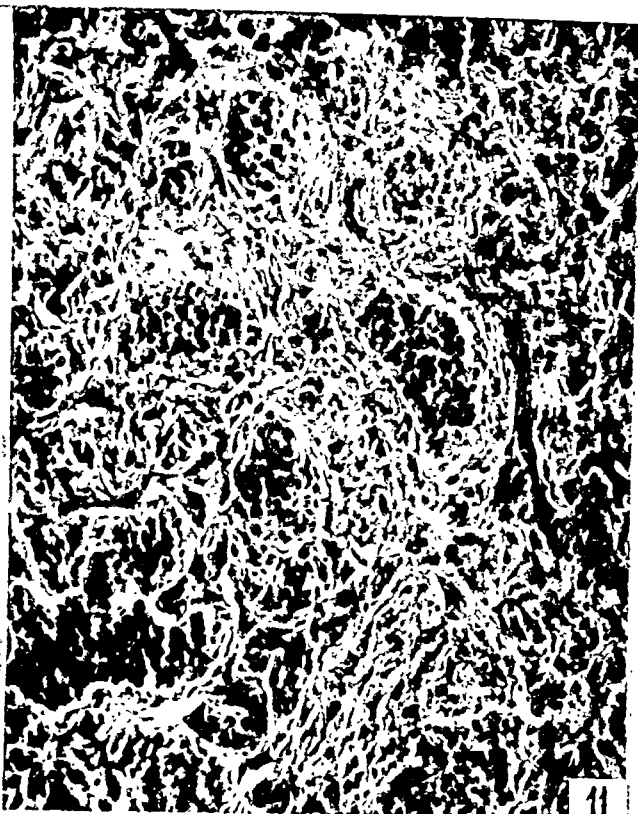
At a late, fibrosed stage, diagnosis must be largely dependent on the clinical history of a pre-existing, possibly congenital "nævus." Laborde (1933) describes the formation of fibrous tissue, with consequent atrophy of the blood vessels and decoloration of the tumour; complete involution, leaving no recognisable mark or only a depressed, scarcely detectable scar, has been observed. Irradiation presumably produces the same sequence of tissue changes, but more rapidly. Excision for diagnosis is very unlikely at this stage. It is of interest that some clinicians have advised the injection of a sclerosing solution for the treatment of angiomas in sites, such as the eyelid, where adequate excision or radiotherapy may present special difficulty (Touraine and Renault, 1933).



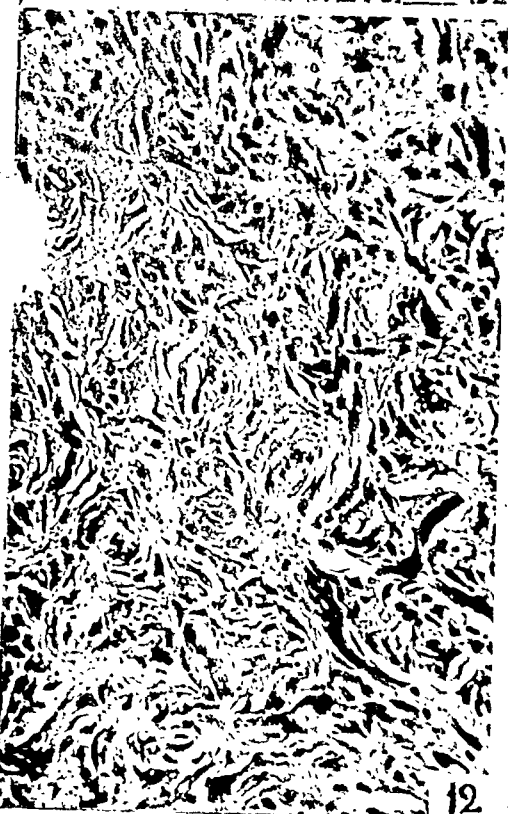




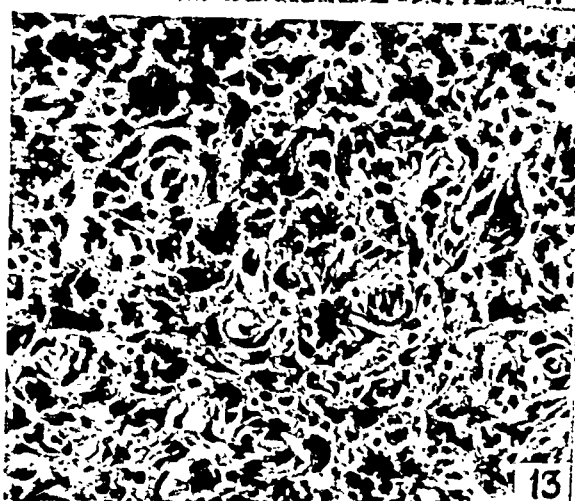
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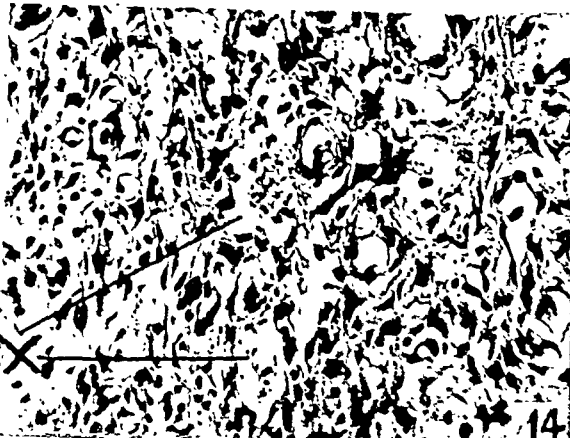
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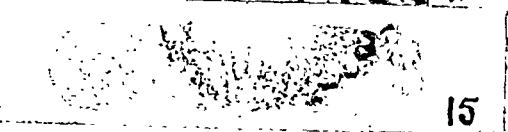
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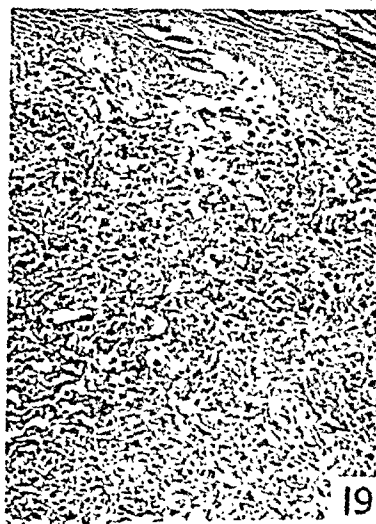
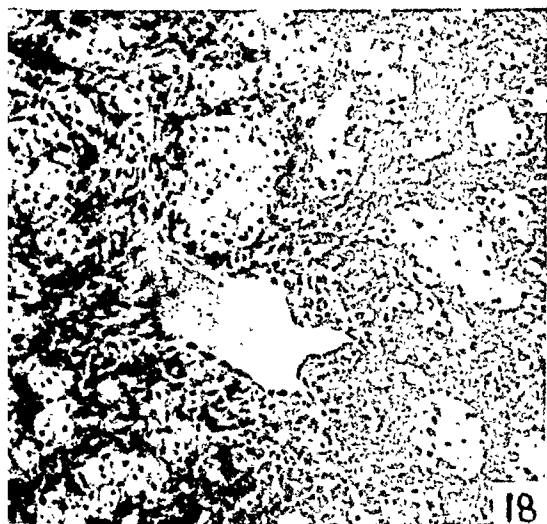
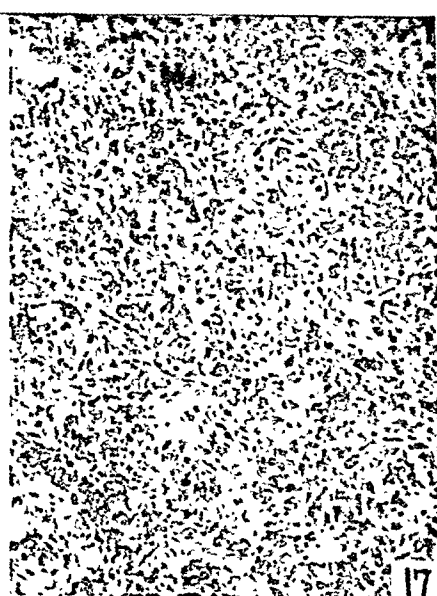
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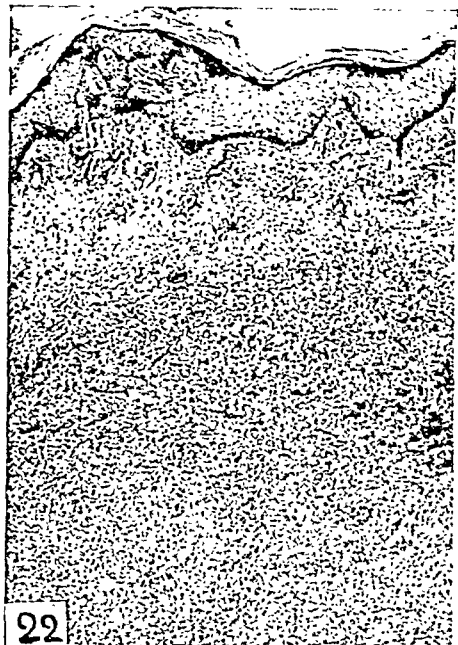


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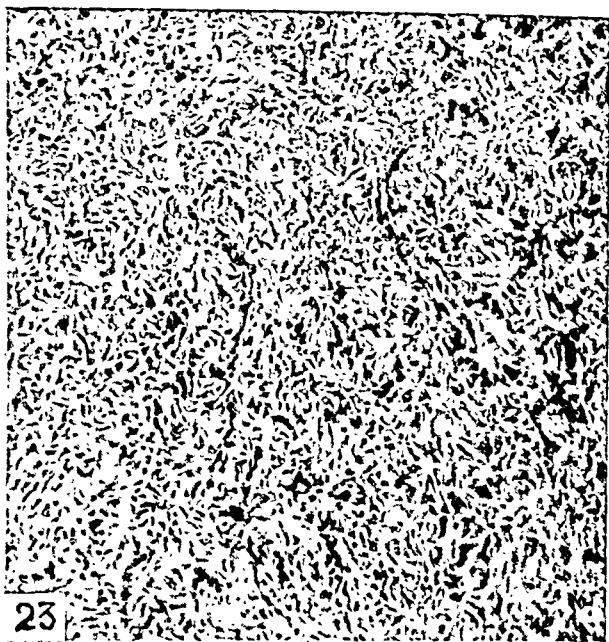


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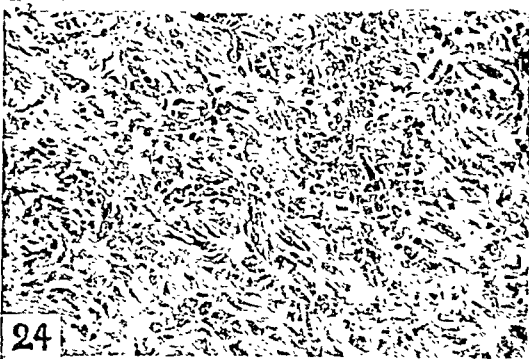




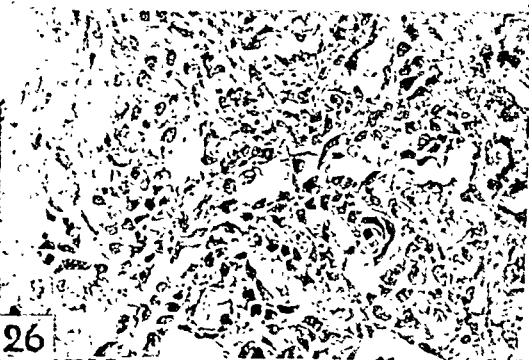
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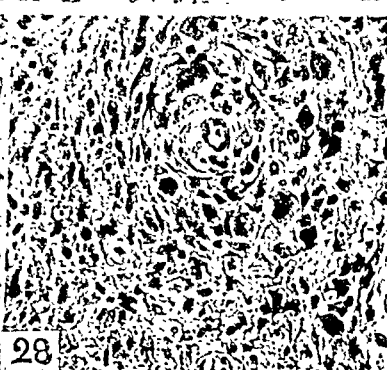
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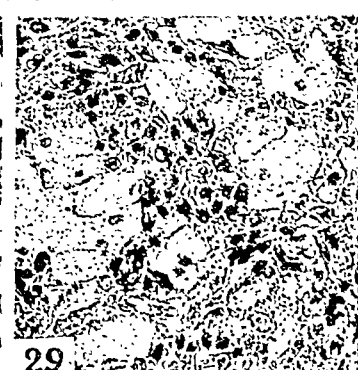
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The benign nature of the sclerosing lesion is implied in its terminology and is emphasised by nearly all observers. Michelson (1933) found no recorded instance of assumed malignant change supported by the later history. This benign character does not necessarily apply to the hæmangio-endothelioma, a relatively rare neoplasm, according to Stout (1943), who has recorded malignant cases in various sites, with metastases and fatal outcome. Dupont (1933) described a sclerosing case as malignant xanthelasmic histiocytoma of the skin, which clinically suggested a malignant melanoma and showed, in addition to many fibroblasts, monstrous multinucleated cells with foamy cytoplasm, like "xanthosarcoma," but growth had been slow, there was no recurrence and the patient was well three years later. Garrett (1924), in the study already referred to, of Bloodgood's xanthomatous tumour material (196 cases) accumulated during thirty years at Johns Hopkins Hospital, reviewed 76 "fibrohæmangiomas" and considered them all essentially benign; in 7 cases, there had been a mistaken histological diagnosis of malignancy—angiosarcoma, fibrosarcoma or malignant melanoma—due to many spindle cells or pigment assumed to be melanin, but only one "recurred" and none metastasised, after local excision. Incomplete removal, in this as in any benign tumour, explains "recurrence."

#### DISCUSSION

Little attention has been given the sclerosing angioma in this country, though one of the earliest and most instructive studies was by McDonagh, in 1912, under the name "nævo-xantho-endothelioma." Some examples are described and illustrated under endothelioma, in *Debatable Tumours* (Harvey, Dawson and Innes, 1940). Gross and Wolbach (1943) of the Harvard School published a comprehensive study of 67 cases. Bailey and Ford (1942) discussed the sclerosing process, with similar pigmentary and lipoid changes, in hæmangiomas of the central nervous system; Sargent and Greenfield (1929) found much blood pigment with foam cell formation in some hæmangiomatous cysts of the cerebellum. Stout (1944) includes the sclerosing form in the skin as a variant of the capillary angioma, though not a very definite one. He notes that foam cell formation may so dominate the microscopical picture that the tumours are usually relegated to a "xanthoma" group, as "fibrous or vascular xanthomas." Many reports in the dermatological literature deal with a single case, with description and terminology relevant only to the stage of sclerosis present. This sclerosing process is a variable and uneven one and, judged by clinical data, may take years or even decades (Gross and Wolbach, loc. cit.) to complete. A patient of McDonagh (loc. cit.), a child born with multiple lesions, some of which were removed for examination at two months and at twelve months, showed complete disappearance of all growths when three and a quarter years old.

The varied and often puzzling histological appearances are more easily recognised if regarded as stages in the sclerosing process of the same tumour type, initially and essentially angiomatous in origin, and not as special tumour forms with unusual features. As with some other neoplasms, it is misplaced emphasis on "unusual" but really secondary features which has produced the multiplicity of names under which the condition is found in the literature. Recognition of the tumour and its variations is also facilitated if its structure is related to embryonal blood vessel formation as well as to the stages of the sclerosing process.

The origin and development of the first blood vessels in the human embryo are obscure and debatable, but one or two points relevant to later activity may be noted. The angioblastic foci in the primitive mesenchyme are described as initially independent, before they link up as networks which will form the systemic circulatory system (Gilmour, 1941). Their growth appears exuberant and even a little haphazard, a biological necessity, perhaps, in what Ewing described as the altruistic tissue of the body. Some foci may remain isolated but active; others grow and then regress, the purely endothelial character of the embryonic vessel wall making modification of channels an easy matter (Dodds, 1938). The possibility of developmental malformation, in a tissue so plastic and so ubiquitous, is therefore considerable, and it is not surprising that vascular nævi form the commonest cutaneous malformation or so-called tumour of childhood. In adult life, they are less frequent, even comparatively rare, except as minute spots in the skin of abdomen or thorax (Illingworth and Dick, 1945), a clinical observation which implies that a large proportion regress and disappear. But single and multiple angiomas are found at any age. The majority are best explained as malformations or "hamartomas" of developmental origin; if first noticed later in childhood or in adult life, a dormant, potential "angiosis" or angioma may have been stimulated to later proliferation or, as Ewing pointed out, a deep-lying lesion, present but causing no previous discoloration of the skin, then becomes manifest. The initial isolation of angioblastic foci in the embryo best explains the multiple lesions which may sclerose, as well as the "benign metastasising hæmangioma." Ribbert's injection experiments (1898) on angioma produced no evidence of connection of the tumour vessels with the adjacent systemic circulation, though other observers assume that enlargement of the cavernous lesion, at least, implies an imperfect junction. Kettle (1917), in tumour tissue from an infant, similar in structure to the scalp lesion of case 8 (Figs. 20, 21), traced a connection of the dilated channels partly filled with proliferated endothelial cells with a neighbouring vein. It is, however, the generally accepted view that the "benign metastasising hæmangioma" is evidence, not of dissemination but of multicentric, benign angiomatous formations. The point is relevant here because sclerosing, pigmented angiomas, if multiple, have been regarded, both clinically and

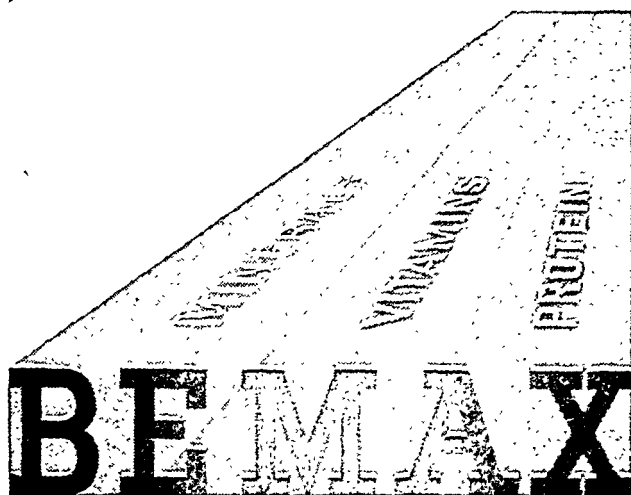
pathologically, as malignant and metastatic. The very rare malignant case, involving several tissues and organs, probably indicates active extension of a cellular focal growth, which has invaded the general circulation. Whether this probability includes the manner of spread of Kaposi's sarcoma need not be discussed here, though this condition may be regarded as a progressive, cellular angiomatosis (Fig. 26), with or without pigment deposit.

While many observers (*e.g.* Fraser, 1920; Shaw, 1928; Kaessler, 1938; Sutton and Sutton, 1939; Englander, 1948) have noted the regression of angiomas, an involution sometimes associated with dentition, puberty or an acute illness, the actual process has been seldom followed, even clinically. Its probability is important, to decide the necessity and the optimum time and type of treatment (Pfahler, 1946; Molesworth, 1933), both debatable points regarding young subjects. The pathologist is concerned mainly with the process itself and the recognition, for diagnosis, of the histological pictures produced in progressive sclerosis. The fibrosis may be preceded by pain and itchiness and a temporary increase in size and pigmentation of a long quiescent angioma, due to successive hæmorrhages and the continued ingestion of hæmosiderin and blood cholesterol by histiocytes. These phagocytic cells become much larger than the endothelial cells which they replace. Later, they are themselves replaced by fibrous tissue, with hardening, shrinkage and decoloration of the area. The factors which cause spontaneous sclerosis and the gradual disappearance of an angioma are uncertain. As already mentioned, most of the reported sclerosing tumours were found in areas exposed to trauma, with the likelihood of repeated small hæmorrhages, or the history noted definite, even single injury. Actual ulceration, in either case, is unusual. Fibrosis may therefore be initiated in this, as in other conditions, by the presence of blood pigment or blood cholesterol, or both, deposited by hæmorrhage in the tumour tissue and acting as irritating foreign materials. There is experimental evidence for this conception (*e.g.* Foot, 1921; Cunningham, 1924; McGowan, 1929; Hieger, 1946). It is interesting that, in rare cases, iron may be deposited in the dermis after iron medication and produce a histological picture almost identical with blue nævus structure; the iron is found both extracellular and in chromatophores, with an associated fibroblastic proliferation (Weiss *et al.*, 1941; Sutton, 1937). The "siderotic nodules" in splenic anæmia, which replace the areas of hæmorrhages in the spleen, show all transitions from recent hæmorrhage to fully fibrosed tissue (Beattie and Dickson, 1943).

It may seem surprising that the angiomatous nature of this pigmented growth has been so generally obscured or unrecognised and the lesion, when melanoma was excluded, described by such names as hard fibroma, fibrosis, histiocytoma, xanthoma and granuloma pyogenicum. It is the more surprising because its real nature was recognised many years ago, notably by McDonagh, in this country

and by Wolbach in America. McDonagh's descriptions noted the vasoformative, capillary structure, the endothelial proliferation merging into a diffuse cellularity, the foam cell formation and pigment deposit and later, the spontaneous disappearance, with fibrosis and flattening of the area, in fact, the classic description of the condition. A diagnosis of fibroma was ruled out, he considered, by the capillary proliferation; the growth was an "endothelioma of the nævus class." Wolbach described a "hæmangio-endothelioma giving the histological appearances of giant-cell xanthoma" as a slow-growing, angiomatous tumour with sclerosis, similar to McDonagh's nævo-xantho-endothelioma and Unna's fibroxanthoma. He concluded that many "multiple tuberous xanthomas," especially congenital ones, were probably hæmangio-endotheliomas. The later, detailed histological study of the sclerosing growth, from the Boston School, by Gross and Wolbach, has already been referred to. Arning and Lewandowski (1911) described the tumour, non-specifically, as a "cutaneous nodule," which might be primarily a fibroma or a post-inflammatory fibromatous lesion, the late, fibrous stage of the granuloma pyogenicum of the dermatologists. They noted, however, the capillary overgrowth, with vessels compressed by the surrounding cellular tissue which was "associated with the capillaries and indeed originated from them." In a study of "tumours of xanthoma type," a group which included the "fibro-hæmangioma," by Bloodgood, Garrett and Smith (1924), all three observers considered that angioma and xanthoma were closely related, if not indeed the same tumour type. In these and in many other descriptions, the angiomatous structure of the lesion is thus accepted or implied, even when much fibrous and xanthomatous tissue is present. Later, however, this latter feature comes to dominate the description and a new term, *histiocytopoma*, was introduced by Woringer (1931) of the Strasbourg school. He laid emphasis on the lipid-laden foam cell and the stages of its formation as the essential feature and described transitions from fusiform cells with no lipid content to the large round foam cell with obvious and abundant lipid ingestion. Numerous case reports of "histiocytopoma" followed Woringer's first report, especially in the French dermatological literature—14 are to be found in volume 40 alone of the *Bull. Soc. fr. Derm. et Syph.* The term histiocytopoma often carries a descriptive affix, such as siderotic (Chatellier and Gadrat, 1936), pseudomelanotic (Diss, 1938), black (Montpellier *et al.*, 1939), or pigmented (Dobkévitch and Marques, 1939). The two cases described by these last observers, however, showed foam cells formed by the ingestion of blood pigment but no fat. Pautrier and Woringer (1933) later restricted the term histiocytopoma to tumours showing a minimum of lipid cells and very near a fibroma; if many foam cells are present, they describe it as xanthoma. This, however, is not an acceptable classification, based as it is on the quantitative and variable presence of only one of the tumour features and ignoring what Mallory (1910) considers the logical basis of classification, the cell or tissue of

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origin. The term histiocytoma is also used by some American dermatologists (Senear and Caro, 1936, 1941; Bernstein, 1939; Sutton, 1942). Senear and Caro (1941) justify their adoption of the term on the ground that colloidal iron, injected pre-operatively into the tumour tissue, was subsequently found ingested by the predominant cells of the area, the histiocytes, but 15 of their 25 reported cases (1936) also showed lipoid-containing phagocytes. We can assume that the angioma produces, slowly, its own "injection" of iron and fat by traumatic or spontaneous hæmorrhages, a process which may also be seen in hæmorrhagic tissue, quite apart from tumour growth. Robb-Smith (1945) considers histiocytoma a more acceptable name for this "benign reticular skin tumour" than sclerosing hæmangioma. His description (1944) suggests the later stages of sclerosis, with yellowish-grey tumours which resemble a fibroma superficially but show, scattered through the collagen, "histiocytes containing lipoids or iron pigment." By most of those who favour the term histiocytoma, however, the phagocytosis is associated predominantly with lipoid ingestion and a positive Sudan III or Scharlach R reaction. Sézary and Lévy-Coblenz (1933) discuss this feature in their paper, which describes tissue changes "From Histiocytoma to Xanthoma."

The introduction of the term "histiocytoma" has clouded rather than cleared the real significance of the tumour structure. Even if we limit the meaning of histiocyte to macrophage, the term histiocytoma would logically include many lesions other than the sclerosing angiomas in which phagocytic activity is present and dominant, whatever the material ingested. The "siderophagic" and "lipophagic" areas in giant-cell tumours of tendon sheath and bone, for example, are shown in Figs. 28 and 29, respectively. If, however, the histiocyte is regarded as the equivalent of a primitive reticulum cell of the mesenchyme with multiple potentiality, a view favoured by many French writers, histiocytoma and reticuloma or reticulo-endothelioma become more or less synonymous terms and, as Pautrier and Woringer (1933) point out, the group would then include such widely diverse lesions as epulis, congenital or acquired, mycosis fungoides, Hodgkin's disease, xanthomatous tendon sheath tumours, etc. We might add other "granulomas" and fat necrosis, and even, as opposed to melano-blastomas, "chromatophoromas," though here, by convention, the pigment implied is melanin. Smith (*loc. cit.*), who did much experimental work on pigment ingestion in tissue cultures, found "really nothing diagnostic about the type of cells that contain the pigment in the xanthomas." It was found in white blood cells, fibroblasts and endothelial cells, though the histiocyte was the most constant and the most striking of the phagocytic cells. The lesion discussed here, however, as one type of pigmented tumour of the skin, even when very foamy in structure, is essentially angiomatous and the "histiocytoma" features—hæmosiderin and lipoid ingestion—though often prominent and diagnostically helpful, are secondary and variable.

There seems little, if any justification for the retention of the term for this tumour type.

The other and older term to which, perhaps, a premature and uncritical hospitality was also extended is "xanthoma." Xanthoma is now generally rejected, by most workers, as a true neoplasm, for it shows no proliferation, no infiltrative or destructive growth and no metastases (Borst, 1924; Wustmann, 1925). Tumour formation, in the sense of increase in size, is due to proliferation of mesenchymal cells *before* lipid ingestion produces the foamy cells, and to the subsequent enlargement of individual cells by this xanthomatous change. As Haagensen (1932) points out, the term xanthoma covers a great variety of disease types, with or without blood lipid disturbance, many of which are not tumours. These foamy or granular-cell "tumours" may be present at birth, as, for example, the "congenital epulis" of the new-born, or they may appear soon after birth or later, as multiple lesions in the skin, the congenital or juvenile multiple tuberous xanthomas. Wolbach, as already mentioned, thought that many of the reported cases of multiple tuberous xanthoma and particularly the congenital ones were probably hæmangiomas. Ellis's (1941) description, clinical and histological, of "necrobiosis lipidica" is very suggestive of another name for this same "tumour," with endothelial proliferation, dilated vessels, fatty cells and healing by sclerosis which left little or no scarring. The jaw and palate lesions are usually and necessarily removed, but many of the cutaneous ones regress without treatment, or persist and even temporarily increase in number. The possible association of these xanthomatous conditions with a metabolic lipid disturbance was rarely investigated or later histories reported, though their spontaneous disappearance was sometimes noted, hastened, in some cases, by a dietetic regime of low fat and calorie intake, even when there was no demonstrable hypercholesterolaemia (Moreland and Dardinski, 1933; Cranston Low, 1948). On the other hand, "xanthoma" may be produced in animals by feeding with large amounts of cholesterol (Weidman, 1927). More chemical investigation is needed, to explain these xanthomatous conditions and relate them to other, histologically similar ones associated with diabetes ("xanthoma diabeticorum"), jaundice, nephritis, arteriosclerosis, etc., or seen in dystrophies such as Gaucher's, Niemann-Pick's and Hand-Schüller-Christian's diseases, which form a group of ill-defined range, described as lipoidoses or lipid histiocytoses. The sclerosing angioma, as such, is not associated with a systemic disturbance, but if multiple and regressing, with extensive xanthomatous change, a metabolic lipid upset may need consideration and exclusion, in differential diagnosis. Where, as might happen, the two lesions co-exist, blood stasis or frequent hæmorrhages in the angiomatous tumour tissue would localise the excess cholesterol in the circulating blood, as Kirch observed (1924).

The consideration of these foamy or granular-cell lesions raises

another interesting and relevant question, that of the "granular-cell myoblastomas of striped muscle." Similar formations in the skin are also considered "myoblastomas," though, as Klinge (1928) pointed out, there is no striped muscle in the skin. Abrikossoff (1926, 1931), who introduced the conception of "excessive regeneration after injury" as the genesis of this "myoblastic tumour," most frequently found in the tongue, admitted this exception. There is a growing rejection of his "myoblastic tumour" (Gray and Gruenfeld, 1937; Willis, 1948b), even for the tongue, where a degenerative change in the muscle fibres can be demonstrated. An explanation for the granular cells in similar formations in the skin might be found in the xanthomatous stage of a sclerosing angioma or, as the element of trauma is stressed for the "myoblastomas" in general, in small hæmorrhages in the dermis, with or without a pre-existing angiomatous basis. The larger, single lesion of the gum or palate, congenital in origin, calls perhaps for further explanation. It might be angiomatous, with extensive and usually complete xanthomatous change, as large angiomas may involve the buccal mucosa, or it might be associated with some lipoid dystrophy, possibly temporary, for later developments after excision have apparently rarely been recorded in these cases in the past. The deposition of lipoids, associated with excessive or, more probably, unbalanced contents of the blood (McGraw, 1933), is more likely in areas exposed to trauma or tension—gums, elbows, tendon sheaths, buttocks—or even in large vessels such as the aorta, as in Cranston Low's case (1910), of multiple xanthomas in a boy of eleven years. The element of trauma, with small repeated hæmorrhages and the deposition of hæmosiderin and blood lipoid in the tissue apparently explains both the xanthomatous change and the initiation of the sclerosing process in the capillary angioma. This study of a small series of the tumour and of many clinically similar, reported pigmented growths emphasises again the necessity of an adequate history and investigation and of follow-up data, to confirm the histological diagnosis, the more so, that prognosis is so different for the two important tumours in this pigmented group, angioma and melanoma.

#### SUMMARY AND CONCLUSIONS

(1) The sclerosing angiomas are difficult to recognise clinically. Histologically, they show wide variations of vasoformative structure, usually with hæmorrhage, hæmosiderin and blood lipoid deposit and varying stages of fibrosis and hyalinisation. Though essentially benign, their pigmentation and occasional ulceration frequently suggest a melanomatous and possibly malignant lesion.

(2) The stage or degree of sclerosing involution produces a histological picture ranging, at the time of examination, from a cellular angiomatous structure to an almost pure fibroma or "xanthoma." This wide range of structure explains the many names under which the tumour is found in the literature. Some of these are discussed.

There appears little justification for the commonest term, "histiocytoma."

(3) Diagnosis of a sclerosing angioma, in the absence of a convincing vasoformative histological pattern, may need confirmation of the hæmosiderin usually present, to exclude melanin. A reticulin stain is also helpful in defining the blood vessels. If the lesions are multiple and show much foam cell formation, that is, a xanthomatous appearance, a systemic metabolic disturbance, with or without hypercholesterolæmia, may need exclusion.

(4) Differential diagnosis includes the consideration of melanoma, in particular, but also of carcinoma, blue nævus, neurofibroma, cutaneous fibroma, leiomyoma and "xanthoma" (localised lipid granulomatosis).

(5) Little attention has been given to the cutaneous sclerosing hæmangioma under this name. Its misleading features suggest that the diagnosis of angiomatous growth needs a point of view more inclusive than the recognition of the ordinary types of blood vessel tumour, whether capillary, cavernous or compactly cellular.

The material studied has been received from a number of sources and my own collection of cutaneous lesions has also provided illustrative cases. I am specially grateful to Dr Helen Russell of the Christie Hospital and Holt Radium Institute, Manchester, for cases with differential staining and follow-up notes, to the late Lieut.-Col. W. H. Harvey of this Laboratory and to Dr Wm. Forbes and Dr A. M. MacDonald of the Pathology Department, University of Edinburgh, for instructive cases from their reporting material. I am indebted to the Carnegie Trust for the Universities of Scotland for generous help towards the cost of illustration. The photographs, with one or two exceptions, were prepared by Mr T. E. Dodds, F.R.P.S., of the University Pathology Department, with much care and interest.

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## THE ROLE OF SURGERY IN THE TREATMENT OF CARCINOMA OF THE CERVIX

By CHARLES D. READ, F.R.C.S., F.R.C.A.S., F.R.C.O.G.

MR PRESIDENT, LADIES AND GENTLEMEN,

I should first of all like to thank you for the honour you have done me in inviting me to address your very famous Society.

My pleasure is the greater in that I recall a very pleasant sojourn in Edinburgh over twenty years ago, during which time I somehow convinced the examiners for the Fellowship that I was safe to practise some form of surgery. I presume that the examination standard must have been considerably raised since that time!

My talk this evening has in very large measure been covered in March of this year in a similar paper read before the New York Obstetrical Society. This will soon be published in the *American Journal of Obstetrics and Gynecology*. To both the New York Obstetrical Society and to the American Journal I would like to make acknowledgment.

In any discussion on the subject of the treatment of carcinoma of the cervix, division of opinion invariably centres around the relative merits of radiation and radical surgery. This generally applies only to cases coming within the category of Stages I and II. There is agreement that almost all Stage III and IV growths are unsuitable for treatment by radical surgery, though even in these it is possible to treat some by a combination of surgery and radiation. In my recent visit to the U.S.A. and Canada I witnessed at the Memorial Hospital in New York, the most ultra radical surgery being performed by Dr Brunschwig—a late Stage III carcinoma of the cervix being treated by a simultaneous performance of hysterovaginectomy, total cystectomy and sigmoid-colectomy with transplantation of ureters and colostomy—a procedure the usefulness of which can only be judged by the passage of time. In respect of surgery we have been interested in the recent publications of Dr Joe Meigs of Boston and of Dr Taussig on the relative merits of the Wertheim operation and of pelvic lymphadenectomy respectively, and it is upon these two aspects of the subject that I wish to speak in the main tonight.

In many clinics the Wertheim operation was abandoned when radiotherapy in the form of radium application and deep therapy became generally established, but at my hospital the radical surgical operation has been practised continuously, but lately in rather carefully selected cases only. The Schauta hysterovaginectomy by the vaginal route has not been employed, because of its neglect of the gland-bearing area, and I personally have had no experience of the operation.

Read to the Edinburgh Obstetrical Society on Wednesday, 19th May 1948.



From a perusal of the records of the Chelsea Hospital for Women, it appears that the first radical abdominal hysterectomy for carcinoma of the cervix was performed by Bonney in 1907, and it must be remembered that at this time there was no adequate alternative method of treatment. The operation was performed with increasing frequency up to the late 1920's by which time radiotherapy, with its low mortality and increasing efficiency, in part supplanted surgery as a method of treatment. I feel, however, that in the present state of our knowledge there is still an important place for surgery in the treatment of carcinoma of the cervix, and my colleagues also believe this.

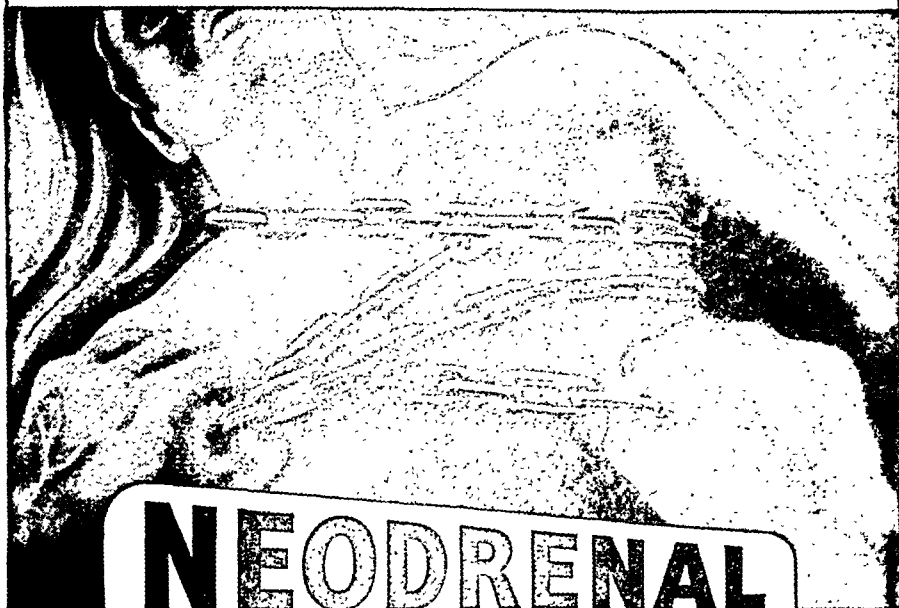
In his "all out" surgical attack on carcinoma of the cervix, Victor Bonney, between the years 1907-36 performed 500 consecutive Wertheim operations. He has since passed the 600 mark. He operated upon all cases which were technically removable, with the exception of a few in whom was present some condition which contra-indicated operation. He began his series in 1907, when no other effective method of treatment was available, and he continued throughout to operate on all operable cases. His operability rate so far as could be judged was 63 per cent. of all cases seen, and his series included Stage I, II and III growths. Unfortunately analysis of the stage of advancement of the growth cannot be made, as this classification was not in existence over the greater part of his series. He found malignant involvement of the regional glands in 40 per cent. of patients operated upon, and of the 500 patients subjected to surgery there were 70 operative deaths, a mortality of 14 per cent. over all.

In my submission, this work of Bonney's represents one of the most valuable clinical research investigations ever made in respect of carcinoma of the cervix. Not only does it show what surgery alone can do in such cases, but it has afforded us the first statistical evidence on a large scale of the incidence of malignant gland involvement. It has also shown that gland involvement is not absolutely dependent upon the stage of the growth in the cervix. While it is generally true that the more advanced the growth the more likely are the glands to be affected, this is by no means always the case, and advanced cases with little or no gland involvement have been frequently encountered, while conversely some early cervical growths have shown extensive gland invasion.

Of the 500 operations, histological examination revealed that in 300 patients the glands were free of growth, and in 200 the glands were involved. The five year cure rate in the gland free cases was 53 per cent., but when corrected 58 per cent., and the corresponding cure rate in the gland positive cases was 22 per cent., or when corrected 23 per cent. It is thus obvious that the prognosis is gravely affected by the presence of carcinomatous deposits in the regional glands. His overall five year cure rate is 41 per cent. of the patients operated upon.

It must be appreciated that these figures for surgery apply only to the 63 per cent. of cases which are deemed to be technically operable.

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There remains the further 37 per cent. of patients who are beyond the hope of radical surgical extirpation of the growth, or in whom age and cardiac or renal insufficiency makes operative treatment inadvisable.

Bonney's figures of 14 per cent. operative mortality are constantly quoted, but it must ever be remembered that this is a mortality rate resultant from an "all out" surgical attack on practically every technically removable growth. A further analysis of his figures shows that his operative mortality in the gland free group is 10 per cent., whereas the gland involved group showed a figure of 20 per cent.

I quote these figures not because I consider the radical abdominal operation in general to be the best method of treatment of cervical cancer, but because I wish to stress the results which surgery alone can accomplish in curing the disease.

A further analysis of Bonney's results, taking into consideration the 37 per cent. of patients not subjected to surgery, shows an absolute cure rate of 25 per cent., or when corrected 26 per cent. He estimates that if the proportion of cases favourable for radiation but unfavourable for surgery because of cardiac or renal disease or adiposity be added, his absolute total saving of life should be in the region of 30-31 per cent.

TABLE I

*Radical Abdominal Hysterectomy (Bonney)*  
500 Cases—1907-1936

<i>Operability Rate</i>	63 per cent. of all cases seen.
<i>Operative Mortality</i>	70—14 per cent.
Gland Free group	300—Operative Mortality—10 per cent.
Gland Involved group	200—Operative Mortality—20 per cent.
Percentage gland involvement—40 per cent.	

TABLE II

*Radical Abdominal Hysterectomy (Bonney)*  
500 Cases—1907-1936

<i>Cure Rate—5 years—All Cases</i>	40 per cent.
Corrected Cure Rate	43 "
<i>Cure Rate, Gland Free Cases</i>	53 "
Corrected Cure Rate	58 "
<i>Cure Rate, Gland Involved Cases</i>	22 "
Corrected Cure Rate	23 "
<i>Absolute 5 year Cure Rate</i>	25 "

But if Cases favourable to radiation but unfavourable to surgery be added, he estimates the total saving of life to be 30-31 per cent.

In none of Bonney's cases was radiotherapy employed routinely either before or after operation.

At this juncture it is interesting to compare the results which were being obtained by radiotherapy. The first reliable published results appeared between 1931-33 (see table). The five workers depicted publish a total of 2,583 patients treated up to 1926 with 614 five year

survivals, *i.e.* a survival rate of 23·8 per cent., and this represented the results in the majority of cases of the use of radium without deep therapy.

TABLE III

*Radium Results Published, 1931-1933*

Year.	Worker.	Patients.	Five Year Survivals.	Per cent.
1931	Healey (U.S.A.) . . . . .	1574	352	22·3
1932	Regaud and Lacassagne (France) . . . . .	317	107	33·7
1933	Gray Ward and Farran (U.S.A.) . . . . .	343	85	24·7
1933	Kelly (U.S.A.) . . . . .	349	70	20

Total patients treated up to 1926 . . . . . 2583  
 Total 5-year survivals . . . . . 614=23·8 per cent.

The latest results published show an improvement in these figures when compared with figures shown in the previous slide (see table). More recently Richards of Toronto has published even better results for radiotherapy.

TABLE IV

*Marie Curie Hospital—London (Hurdon) 1942. Radium and X-ray Results  
Cancer of Cervix*

Classification.	Stage I.	Stage II.	Stage III.	Stage IV.	Total.
No. examined . . . . .	40	174	455	167	836
No. treated . . . . .	40	174	455	138	807
Five year survivals . . . . .	32	107	143	10	292
Died of cancer . . . . .	6	65	308	127	506
Died of intercurrent disease . . . . .	2	2	4	1	9

TABLE V

*Marie Curie Hospital—London (Hurdon), 1942  
Five Year Survival Rate—Carcinoma of Cervix*

	Stage I.	Stage II.	Stage III.	Stage IV.
Relative . . . . .	80 per cent.	61·5 per cent.	31·4 per cent.	7·2 per cent.
Absolute . . . . .	80 per cent.	61·5 per cent.	31·4 per cent.	6 per cent.

*Ten Year Survival Rate*

Stage I.	Stage II.	Stage III.	Stage IV.
63·6 per cent.	41·9 per cent.	22·4 per cent.	2 per cent.

From the foregoing, even the most biased surgical enthusiast must admit that over all and in general the results of radiotherapy compare more than favourably with those of surgery, but in spite of either method of treatment a considerable proportion of patients die from the disease. The problem now arises, can we salvage the lives of any of those patients who are destined to die even after adequate radiotherapy? In addition, is it ever desirable to employ surgical means without previous radiotherapy?

In a survey of the statistics relating to carcinoma of the cervix at the Chelsea Hospital for Women over the past twelve years, I find that the operation has been performed on 96 occasions and that 8 patients did not survive the operation, an operative mortality rate of 8.3 per cent. Further investigation reveals that this represents 14 per cent. of all the patients presenting themselves with the disease. The highest operation rate in any one of these cases was 20 per cent. and the lowest 9 per cent. Before the year 1936 on an average 55 per cent. of the patients so presenting were treated by the Wertheim operation with an operative mortality of roughly 14 per cent. The year 1936 is taken as the dividing line, as it was in this year that the majority of the members of the Honorary Staff of the hospital decided to be more selective in their indications for the radical operation. It is interesting to note that just on 50 per cent. of the mortality in the recent twelve years period has been incurred by the few colleagues who have not been so selective in their indications for surgery. Had this careful selection been exercised it is fair to assume that the operative mortality would have dropped to about 4 or 5 per cent.

This is in accordance with Meig's experience. Indeed he publishes 91 consecutive operations without a post-operative death. My colleague Frank Cook and I, working independently at the Chelsea Hospital for Women, and in our other hospitals and nursing homes have performed Wertheim's operation 205 times with 6 operative deaths—a mortality rate of 3 per cent. This is not a tribute to any exceptional operative skill but to a careful selection of cases, improved anæsthesia, the use of blood transfusions and plasma infusions, the use of penicillin and the sulpha drugs and not least of all to good nursing.

It will thus be seen that since 1936 on an average, 14 per cent. of the patients with carcinoma of the cervix have been subjected to the Wertheim operation—9 per cent. being the lowest in any one of the years and 20 per cent. being the highest rate. Previous to this 55 per cent. of all cases presenting were operated upon, whereas Bonney in his own personal series considered that he operated upon 63 per cent. of the patients presenting.

From the above it appears that operative treatment is now embarked upon in about one case in seven, whereas originally every alternate patient was subjected to surgery. Our selection of cases for the radical operation is largely confined to the type of case in Table VI.

## TABLE VI

*Indications for Wertheim Hysterectomy To-day*

1. Radio-Resistant Growths proved either clinically or cytologically. (Biopsy positive).
2. Columnar Celled Carcinoma of the Cervix.
3. Stenosis of Vaginal Vault.
4. Fibroids or Ovarian Cysts complicating Cervical Cancer.
5. Salpingitis complicating Cervical Cancer.
6. Refusal of Radiation by the Patient.
7. Pregnancy complicating Cervical Cancer.

*Radio-Resistance.*—So far as we know at the moment the most reliable method of determining radio-resistance is on clinical grounds, and we have all experienced the growth which fails to improve clinically after radiation or which after appearing to heal breaks down relatively quickly. Repeated biopsies confirm the diagnosis of resistance. Many attempts have been made on histological grounds at an early stage of radiation to determine early resistance, and Koller working at the Royal Cancer Hospital and in association with the combined Cancer Clinic of the Chelsea Hospital for Women and the Royal Cancer Hospital, bases his criteria of radio-resistance on the effect of irradiation on mitosis as well as with its effect on surrounding connective tissue reaction. So far we have chosen to formulate the diagnosis of resistance on either clinical or biopsy evidence entirely.

*Columnar Celled Carcinoma of the Cervix.*—So far, we have found these adenocarcinomatous growths very resistant indeed. At the Chelsea Hospital for Women only 10 per cent. survived over five years after radiation. Maliphant of Cardiff finds 14 per cent. five year survivals, and Professor Windeyer from the Middlesex Hospital, reports about 14 per cent. five year survivals. In a small series of 11 such cases which I have followed up after the Wertheim operation, so far 4, or 36 per cent. are alive and well after a period of five years. In this respect also we have noted that the squamous endocervical growth appears more resistant than the more common exocervical growth.

*The Presence of Large Fibroids, Ovarian Tumour or Salpingitis* in our opinion always contra-indicates radiation, and all such cases are treated surgically if the patient's condition permits of this.

*Vaginal Vault Stenosis due to Congenital or Acquired Lesions* makes adequate radium application impossible, and *Refusal of Radiation* by the patient is occasionally encountered.

*Pregnancy Complicating Cervical Neoplasm* is a serious matter and opinions vary as to the best method of treatment. Technically the operation during pregnancy is more difficult as the vascularity of the parts makes oozing more troublesome, though this is to some extent offset by the pliability of the tissues. I have performed Wertheim's operation on three occasions during pregnancy, and one of these patients has survived eight years. The other two patients died within one year of widespread recurrence.

## WERTHEIM'S OPERATION AFTER PREVIOUS IRRADIATION

On forty-two occasions I have performed the operation after previous radiation by radium alone, or by a combination of radium and deep X-ray therapy. The intervals between radiation and operation have ranged from one week to fourteen months. This latter was an unusual case which had been fully radiated by local radium and two full courses of deep therapy under the care of Professor Windeyer of the Middlesex Hospital. The patient persistently gave a positive cervical biopsy for adeno-carcinoma, and in the end he asked me to attempt a radical abdominal hysterectomy. This was accomplished without any real difficulty together with a thorough clearance of the gland-bearing area. The cervix showed undoubtedly active adeno-carcinomatous changes, but the glands were negative for growth and I am quite sure that they had never been involved. In the main, previous radiation does somewhat magnify the technical difficulties of the operation, but provided the growth still conforms to Stages I or II, in my experience it is always removable. In my opinion it is more than justifiable to attempt such cases, as the alternative to operation is death.

## RESULTS OF WERTHEIM HYSTERECTOMY ON CASES SELECTED AS UNSUITABLE FOR RADIATION OR FOUND TO BE RADIO-RESISTANT

During the years 1936 to 1941 in the Chelsea Hospital for Women 54 operations were performed in such cases. In all there were 34 Stage I and 20 Stage II growths, and at the end of five years 24 patients, or 44·4 per cent. of the total were known to be alive and well. Six were lost in the follow-up during the first three years of the war. If these be excluded it will be found that 50 per cent. of the patients followed-up were alive and well. There were three operative deaths in the series, a mortality rate of 5·5 per cent. It must be remembered that most of these cases were selected as being either unsuitable for radiation or as being proved radio-resistant cases. The number who would have survived without operation is impossible to assess.

TABLE VII

*Results of Wertheim's Operation at the Chelsea Hospital for Women  
for the Years 1936-1941 inclusive*

	Stage I.	Stage II.	Stages I and II.
Number of Cases treated . . . . .	34	20	54
Number alive at end of five years . . . . .	14·41 per cent.	10·50 per cent.	24·44 per cent.
Lost in follow up . . . . .	5	1	6
Number alive after five years excluding lost cases	14·48 per cent.	10·53 per cent.	24·50 per cent.
Operative deaths . . . . .	...	...	3
Operative mortality . . . . .	...	...	5·5 per cent.



## THE REGIONAL GLANDS

So far as we can assess we have come to the conclusion that the rate of carcinomatous gland involvement is approximately as follows :—

Stage I . . . . .	20-25 per cent.
Stage II . . . . .	30-35 „
Stage III . . . . .	40-50 „
Stage IV . . . . .	Over 60 per cent.

These figures are based on material obtained from the Wertheim operation, from the operation of lymphadenectomy without removal of the uterus and from autopsy material and these figures appear to agree with some other observers.

It would appear obvious that treatment by radium alone using vaginal applicators only, can never hope to give adequate radiation to the lymphatic field of the pelvis. Some workers even question the efficiency of deep ray therapy in this respect. At the risk of incurring the enmity of my radiotherapy friends here, I make so bold as to suggest that this ability to sterilise the pelvic lymphatic field of carcinomatous deposits is not so great as many of them think. I feel so strongly about this that I often wonder if the improvement in the results of radio-therapy are not due more to improvements in the details of application, screenage and dosage of the radium rather than to the addition of deep X-ray therapy. Indeed the latest five year report of the Holt Radium Institute in Manchester shows better results in Stage I and II growths with radium alone than with combined radium and deep X-rays.

TABLE VIII

*Holt Radium Institute (Manchester) 1945. Cancer of Cervix. 771 Cases. 1932-1939.  
Radium Treatment with and without X-ray Therapy*

Technique.	Stage I.		Stage II.		Stage III.		Stage IV.	
	No.	Five Year Survivals.	No.	Five Year Survivals.	No.	Five Year Survivals.	No.	Five Year Survivals.]
A. Radium and X-rays .	23	62 per cent.	224	44 per cent.	212	29 per cent.	55	20 per cent.
B. Radium alone .	35	76 per cent.	117	49 per cent.	58	25 per cent.	27	8 per cent.

However, their numbers are relatively small, and one must confess that these results are at variance with those usually shown for other centres.

In this respect also I have had some experience of performing lymphadenectomy after a full course of treatment by radium and deep X-rays. I have found a cured cervix with negative biopsy in

association with positive lymph nodes apparently unaffected by the deep therapy. In all those cases in which the lymph nodes have proved negative for carcinoma they have been so mobile and so easily removed that I cannot believe that they have ever been involved. I have never yet removed adherent lymph nodes which have been obviously sterilised by radiation and which have been proved to be free of growth.

Likewise I have yet to see a recurrence following the Wertheim operation successfully treated by deep therapy, and this has also been Mr Bonney's experience.

We must accept the fact that in up to 80 per cent. of Stage I growths the glands are unaffected, in up to 70 per cent. of Stage II growths they are free and in upwards of 50 per cent. of Stage III growths there is no malignant involvement. Is it in these gland-free cases that the radiotherapist obtains his successes? No one will doubt that the adequate application of radium will cure the majority of the local cervical growths, but to my mind it is not yet proved how efficient is deep therapy in eradicating the disease from the gland-bearing area. I feel with Dr Morton and Dr Taussig, both of America, that there is a place for lymphadenectomy in selected Stage III cases which have been cured locally by radium, and I feel that such a procedure could well be extended to include Stage II cases and selected cases of Stage I growth. In such cases the operative mortality is negligible, and my colleagues and I have decided to extend the practice of lymphadenectomy until such time as improvements in deep therapy or some other more effective method of treatment makes the procedure unjustifiable and unnecessary.

### TECHNIQUE OF THE WERTHEIM OPERATION

Before my concluding remarks it perhaps will interest you to outline a few of the technical modifications of the Wertheim operation practised in our hospital. Anæsthesia is obtained by the use of intravenous Pentothal followed by gas and oxygen combined with spinal analgesia using light percaïne intrathecal solution. Recently we have tried the use of gas, oxygen and curare, but so far this has not proved popular. Some of us perform the lymphadenectomy early in the operation, immediately after making certain that the bladder can be satisfactorily displaced downwards. One of my colleagues, Aubrey Goodwin, practices lymphadenectomy early in the operation, sweeping the glands medialwards and leaving the iliac and obturator lymph node chain attached to the uterus throughout. This early attack on the lymph glands facilitates early exposure of the ureters and uterine vessels, allows of better hæmostatis and has the psychological advantage in that it gives the surgeon a sense of completion as soon as the uterus with its attachments has been removed. I also have the impression that operative shock is somewhat lessened.

At least the upper half, and preferably the upper two-thirds of the vagina, are removed, and if this clearance be effected vaginal recurrence is almost unknown. The vaginal vault is left open for drainage purposes and the sub-peritoneal raw area is lightly packed with penicillin gauze, one end of which passes through the vagina. This gauze is removed in thirty-six hours. Plasma infusion or blood transfusion is practised in every case as a routine and the choice of solution depends upon the amount of blood lost.

The ureters and bladder are treated with the greatest gentleness and respect, and this is especially important in the post-radiation cases. Over the past twelve years the incidence of post-operative urinary fistulæ has been 3.1 per cent.—a figure which compares favourably with that of fistulæ following radiotherapy.

### CONCLUSION

I trust that I have not given the impression that I do not appreciate the value of radiotherapy, but I do feel that there has lately been a tendency to take a broader view of the whole subject and to treat each case on its merits. In recent years radical surgery for the condition has tended to be underrated in its usefulness. The operative mortality in properly selected cases should not exceed 5 per cent., and should never reach the high figures sometimes quoted. The figures given for radiation always tend to favour that form of therapy, as the five year results are always described as "survivals" and not as "cures." Indeed a large percentage of five year radiation survivals are literally dying of cancer of attenuated virulence. The ten year survival rate shows a very appreciable drop, and even after this time a considerable percentage of patients die of the remote sequelæ of radiation. In following up these post-radiation cases the interpretation of thickening and infiltration is difficult to assess. The radium enthusiast calls this "fibrosis," the surgical enthusiast designates it as "recurrence," and the honest observer simply states that he does not know. After the Wertheim operation any thickening denotes recurrence, and the falling off in the figures of ten year results is not nearly so great as in the case of radiation. Bonney estimates that between five and ten years he loses a further 10 per cent. from recurrence.

Let me again stress that in my view in the present state of our knowledge, the routine treatment of election for the average case of cancer of the cervix is by radiotherapeutic means, but that in certain selected cases there is a place for surgery which in these cases offers the best prospect for the patient. In addition I suggest that the more extensive practice of lymphadenectomy, especially in Stage III cases, might improve our results. It would at least enable us to assess the real value of deep therapy on the pelvic lymphatic glands if it were practised as a routine after a course of such therapy.

I submit that the absolute cure rate in carcinoma of the cervix can

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The same might be true of cervical cancer and a new approach to its histological study was necessary. Possibly the observation of the irradiation effects in successive biopsies might prove a valuable field of investigation. It was difficult to envisage any great increase in radium range in the near future, apart possibly from improved applicators, with more efficient screening of the bladder and rectum. It was the need to avoid damage to these organs which chiefly restricted the dosage.

In view of the failure of radium to affect malignant cells beyond 3 cm., the question arose of supplementing the radium treatment with X-rays. When this was first attempted, the whole pelvis was irradiated and it was not uncommon for necrosis to develop in the tissues which had already received a high dosage from radium. It became obvious that if X-ray treatment was to be really beneficial, it must be closely aligned to the radium treatment. Patients with cells just outside the effective range of radium were far more likely to benefit from X-rays than patients with cells far out in the pelvis, for these latter advanced cases frequently had distant metastases as well. In order to try to align the two methods of treatment, the X-ray fields were planned from the radiographs showing the position of the radium in the uterus, but when packing was introduced the uterus might be greatly displaced to one or other side of the pelvis and might be displaced upward to a considerable extent. These difficulties could to some extent be overcome by the use of special radium applicators, such as those devised by Richards of Toronto.

X-ray therapy alone would remain an unsuitable method of treatment until much more powerful apparatus became available.

Professor McWhirter believed that surgery was the most effective method of treating cancer when it was early and localised. Unfortunately, by the time patients sought advice, the disease was often no longer suitable for treatment by surgery. In criticism of some of the claims for surgical treatment, it must be pointed out that a number of factors operated to produce a favourable selection of cases. For example, the patients submitted to surgery were usually in good condition, not unduly obese and not too old, while of course the restriction of the operation to Stage I and early Stage II cases was again a most important point. Because extensive lymphadenectomy must always remain a piecemeal dissection, he thought it unlikely that this practice would greatly improve the eventual prognosis. He agreed that it was true that the results might be good where lymphadenectomy had been carried out but lymphadenectomy was only carried out in early suitable cases. The principle was certainly contrary to the current Edinburgh practice where dissection of the axillary glands had been abandoned in cancer of the breast and where abandonment of gland dissection in testicular tumours had resulted in a ten year survival rate of all patients without chest metastases of 63 per cent.

He did not believe that an inoperable case could ever be rendered operable by preliminary irradiation, although he believed improvement might be obtained by means of post-operative irradiation with very high voltage X-ray apparatus, and pre-operative irradiation in operable cases might be of benefit.

In a review made some time ago, the five year survival rate in Edinburgh was 29 per cent. of all cases referred. In the most recently analysed cases, the five year survival rate was 34 per cent. In the calculation of these survival rates, no case was omitted from the total for any reason whatsoever. He believed that these figures might be improved by the use of surgery where the

disease was early and where the tumour was shown to be radio-resistant, and he thought a serious attempt should be made by histologists to recognise resistant tumours, so that the appropriate treatment might be given initially. In Stage II and Stage III cases, supplementary X-rays might bring about considerable improvement in the results, provided the radium and X-ray treatment could be suitably integrated. He thought it unlikely that any real improvement would ever be obtained in Stage IV cases, where only palliative treatment was indicated.

*Dr Douglas Miller* said he would like clarification of certain points in regard to Mr Read's paper. For example, in an early case of cervical cancer, technically suitable for radical surgery, would Mr Read rely entirely on operative removal, or would he prefer radiological attack as well? If the latter, would he favour employing radiotherapy as a preliminary measure, or as a post-operative supplement? Did Mr Read believe that radiotherapy had any real effect upon glandular metastases? His own opinion was sceptical of any such effect.

In regard to Professor McWhirter's paper, Dr Miller commented that his own experience with the use of intra-uterine radium prior to the surgical extirpation of cancer of the uterine body had been rather favourable, and he had been surprised that Professor McWhirter had doubts of the value of this sequence in corporeal cancer. He would like to ask Professor McWhirter whether he believed there was any real justification for palliative X-ray therapy in Stage IV cervical cancer. In Dr Miller's cases this had been associated with such severe skin reactions, much bowel distress, and such general malaise with depression of spirits that he was doubtful whether it was worth while.

*Dr Fahmy* said that it would appear that a case had been made out for surgery in some instances of really early carcinoma of the cervix—*i.e.* a mobile uterus with a doubtful cervix, which proved to be carcinomatous only on histological study of a piece removed. Mr Read's figures showed that even in Stage I cases regional glands were involved in as high as 20 per cent. Professor McWhirter stated that the maximum range of effective radium was 3 cm., and so it would seem that at least 20 per cent. of Stage I cases would be ineffectively treated by radium alone. A number of operators had been carrying out lymphadenectomy because the histological examination of some of the glands removed at operation showed the presence of carcinoma cells even after the patient had been treated by both radium and deep X-ray therapy. It was this knowledge which kept in doubt the question of the wisest method of treatment in Stage I and Stage II carcinomas. Late sequelae from radiotherapy were often distressing and serious, and this aspect of treatment must be kept in mind when the decision for treatment in any one case was finally determined.

The Wertheim operation was one which could only be mastered by very considerable experience; but safer anaesthesia, better pre-operative and post-operative care should lead to better results in experienced hands. As Professor McWhirter said, it might be that the final decision in regard to treatment would only be possible when histological study could definitely determine whether the carcinoma to be dealt with was radio-resistant or radio-sensitive.

*Dr Clifford Kennedy* said he would like to be informed whether it was possible to lay down any criteria for the selection of cases for iliac lymphadenectomy. If 20 per cent. of Stage I cases showed glandular involvement it

seemed difficult to frame any sound indications for the exclusion of any patient from this procedure. Why had the practice of preceding the radium treatment by deep X-ray therapy been given up? This had at one time been the standard method in Edinburgh. How did the lecturers consider cervical cancer should be treated during pregnancy? He would like to postulate two types of case: (a) Stage I or Stage II at three months, (b) Stage I or Stage II at term.

*The President, Dr W. F. T. Haultain*, after welcoming Mr Read as the guest of the Society and thanking both him and Professor McWhirter for their interesting discourses, said he had recently had the instructive experience of watching the 117th consecutive radical operation for cervical cancer by Meigs of Boston, who, at that time, had had no fatalities; he was sorry to hear from Mr Read's paper that he had now had one fatality in 121 cases, but this truly seemed a wonderful record. He thought that the Edinburgh figures in regard to cervical cancer were probably comparable to those of Manchester, where a slightly more favourable response had been seen in 1930-35 (when radium alone was employed) than in 1935-40 (when radium and X-rays had both been used). He wondered if nulliparity in some way influenced the prognosis unfavourably in cervical cancer, as in looking through statistics acquired during ten years in his ward at the Royal Infirmary he had not found a single five year cure in a nullipara, in fact nearly all had died within eighteen months of being first seen. He would like to ask Professor McWhirter who had referred to Gordon Richards' excellent results in Toronto, if Richards was still using the perineal route as well as others in his radiational treatment.

*Dr J. C. Clark, Professor Margaret Fairlie, Dr R. De Soldenhoff and Professor R. J. Kellar* also spoke.

*Professor McWhirter*, replying, said that it was true that metastases in the regional glands would not be affected by radium but it was wrong to conclude from this that radiotherapy was much inferior to surgery in treatment. The five year survival rate of good radiotherapy and of good surgery was essentially the same in operable cases. He admitted that on a ten year survival basis, there might be a bias in favour of radical surgery. If average radiotherapy and average surgery were compared, he believed the bias would be in favour of the former. While surgery could not be used in the more advanced cases, radiotherapy could still be given with some prospect of success, so that taking all the cases together, radiotherapy remained the better method of treatment.

He emphasised again the special place for surgery in radio-resistant growths at an early stage and the necessity for the pathologist to try to distinguish radio-resistant tumours. With an early radio-sensitive tumour, he believed that radio-therapy should still be used, even although the case technically was suitable for hysterectomy.

He agreed that the results hitherto obtained with the addition of X-ray therapy had been disappointing and that the skin reactions produced were often very distressing to the patient. Indeed, this was the chief reason for X-ray therapy being abandoned. When new high kilo-voltage apparatus became available, the use of X-rays would require to be reconsidered.

He believed that Richards had now given up the use of the perineal field in the treatment of cervical cancer.

*Mr Charles Read*, replying, said he did not think the surgeon and the radiologist were poles apart in this controversy. He agreed with Professor

McWhirter that a five year survival in a surgical school would show little difference between hysterectomy and radiation but that a ten years' survival standard would show a bias in favour of surgery. He suggested that the shorter period flattered the radiological method, since a palpable thickening felt vaginally after hysterectomy was always interpreted as recurrence, whereas a similar thickening in a case treated by radiotherapy was looked on as fibrosis, although such a fibrotic area might well enclose cancer cells which were only temporarily inactive.

Nevertheless he agreed that the vast majority of cases of cervical cancer could and should be treated radiologically in the first place, with later pelvic lymphadenectomy. His present attitude was to do this latter operation in all Stage III cases, with possible extension to Stage II and even Stage I cases, progressively accumulating data, and later, after say 1000 cases, analysing the data to form new policies. He did not think it possible to select the cases of Stage I cancer which would show glandular metastases.

In regard to the assessment of radio-resistance, he referred to the work of Ruth Graham and of Ayre in respect of the recognition of this condition from cytological investigation of vaginal or cervical smears. If this work was accepted it did hold out very good prospects for the selection of the cases for hysterectomy.

The Wertheim operation called for a high degree of technical skill, and for considerable training. The skill could be acquired, and its acquisition was a sound surgical discipline. Once a gynaecologist was able to do a Wertheim operation, he need fear no surgical adventures within the pelvis, and was a better gynaecologist. An additional argument in favour of the operation was the fact that it was often possible to conceal from the patient (though not from her relations) the exact nature of her condition, to her eventual comfort. He was forced to admit that the operation was nevertheless unsatisfying in regard to the conviction that the disease had been quite eradicated. No matter how carefully the iliac arteries were stripped of glands, he always felt that a spider's web of lymphatic vessels permeated by malignant cells must be left behind. For a solace to such uneasiness, he looked forward to the day when deep X-ray therapy could be safely and effectively employed.

Meantime, he felt that X-rays were uncertain and sometimes dangerous. It was his experience that superficial lymph gland cancer, as in inguinal metastases from cancer of the vulva, was very seldom radio-sensitive. It therefore seemed advisable to maintain an attitude of scepticism in regard to deeper, less accessible glandular cancer. The dangers of deep X-rays had been accentuated in the discussion and he would like to confirm that his experience was similar. Severe proctitis, sometimes lasting as long as eighteen months, occurred in 15 per cent. of cases, while fistulae and strictures were not uncommon, though it was hard to tell how many of these were the effects of the growth itself rather than its therapy. On the other hand, he had heard good reports in the United States of treatment by X-rays alone, using various types of perineal or vaginal concentration applicators. He had also seen the pelvic lymph glands attacked by very long radium needles inserted *per vaginam*. He himself felt this method to be dangerous from possible damage to strictures traversed by the needle, but Corscaden spoke confidently of the technique.

Preliminary radiation of cervical cancer did not make subsequent hysterectomy more difficult unless an interval of more than three weeks elapsed



between irradiation and operation. In the latter event, the parametrium might be found to be œdematous and hyperæmic, the vessels were less ready to retract when cut, the ureters were more difficult to dissect, and their blood vessels more liable to damage, with a greater chance of sloughing.

He did not favour radiotherapy prior to operation in cancer of the uterine body. At the Chelsea Hospital, a recent survey had shown that in this condition surgery combined with radium showed a survival rate of 50 per cent., while surgery alone showed 61 per cent. However, he thought there might be a profitable field for the application of local radium to the vaginal vault following a hysterectomy carried out for corporal cancer.

In respect of the question regarding cervical cancer complicating pregnancy, he would personally advise for the Stage I cancer in early pregnancy an immediate Wertheim hysterectomy, with the pregnancy *in situ*. At term, he suggested that a caesarean section should be carried out, after which the operator should proceed to a Wertheim hysterectomy after closing the uterine incision with a few mattress sutures. He did not favour the radiological induction of abortion for such cases as a preliminary to fuller treatment either surgical or radiological. Whilst he had the greatest respect for those who, on religious grounds, would criticise his neglect of the child's survival, he was unrepentant.

## QUARANTINE FOR PLAGUE IN SCOTLAND DURING THE SIXTEENTH AND SEVENTEENTH CENTURIES

By JOHN RITCHIE, M.B., Ch.B., M.R.C.P.E., D.Ph.

DURING the sixteenth and, at least, the earlier part of the seventeenth century, the bulk of Scottish overseas trade was with France, Flanders and the Baltic States.<sup>1</sup> These countries, in common with the rest of Europe, were subject to periodic outbreaks of plague, and the protection of our seaports against the introduction of infection was a matter of constant concern to the Scottish authorities. This was no easy task. Scotland was a small country, poor and sparsely populated. War with her more powerful neighbour, diversified by domestic quarrels, absorbed much of her energy, and when both these means of self-expression were lacking bitter religious controversy was usually available to replace them. Even in times of relative peace the ordinary law was administered with difficulty in many parts of the kingdom; to enforce the special and generally onerous enactments necessary for the control of plague was often practically impossible. Yet some sort of defensive mechanism had to be devised, and it may be of some interest to discuss one of the methods designed to control the ravages of a devastating epidemic disease at a time when accurate knowledge of its etiology and method of spread was non-existent.

The responsibility rested primarily on the Privy Council of Scotland which was, in effect, the central health authority of the period, but the actual administration of its orders was normally the duty of the town councils of the seaports, to whom powers were generally delegated and by whom they were sometimes assumed. For extra-burghal districts and for small burghs, whose councils might lack the resources and the authority necessary to enforce the quarantine regulations, commissioners were often appointed, with powers to enlist citizens and to use any force necessary to ensure that the law was obeyed.

In an age when the speed with which administration functioned depended largely on the rate at which a messenger could ride, it was fortunate that the majority of the Scottish ports, and, in particular, Leith, the largest among them, were within fairly easy reach of the capital. Along the shores of the Firth of Forth and the adjacent coast from the eastern extremity of Fife to Eyemouth, close to the English border, lay a number of towns with harbours large enough to accommodate the small trading vessels of the period. All these were sufficiently near Edinburgh to permit of news about the arrival of suspected vessels reaching the Privy Council fairly quickly except, indeed, from Eyemouth which, according to Thomas Tucker who

Read to the Scottish Society of the History of Medicine on 18th June 1948

made a survey of the Scottish ports in 1656, "gave occasion of much deceit"—at least in the matter of landing contraband cargoes, the question with which he was specially concerned.

It was fortunate also that there are in the Forth—as at Venice and Marseilles, two of the first European ports to establish quarantine—a number of islands to which ships could be sent for detention and disinfection. Inchcolm seems to have been that most frequently used; Inchkeith, Inchgarvie and Cramond Inch were also utilised. On one occasion at least a ship was ordered to go into quarantine at the May. There was also a station on the mainland at Newhaven, sometimes used for the final disinfection of people who had been employed in cleansing infected ships, sometimes for isolating travellers who could not conveniently be sent to the islands. Occasionally ships went through their quarantine at their port of arrival, if the authorities thought that might be done with safety.

It would, of course, be wrong to suggest that any regular and permanent service was established. It was not until much later that the provision of machinery for prevention of disease, to be maintained even though there were no obvious or immediate threat to the public health, was recognised as a duty of the State. The regulations and orders regarding plague that were made from time to time during the fifteenth, sixteenth and seventeenth centuries were operative only during the outbreak that evoked them. When the crisis had passed, they, along with the protective measures that they had authorised, fell into abeyance. As soon as the next epidemic seemed imminent the service had to be improvised afresh.

But if no sanitary code was created a useful tradition of service was evolved, as the authorities came to recognise the steps that, according to the ideas of the time, should be taken. It was often impossible to ensure that these steps were taken effectively, but that was due to the inadequacy of the administrative machinery available.

The earlier regulations, admittedly, do not seem specially useful. In 1538, when trade with England was stopped on account of an outbreak of plague on the borders, letters were sent to all seaports on the north and south shores of the Forth directing that no Englishman coming by sea was to be admitted.<sup>2</sup> This appears to have been an attempt to impose a complete barrier to traffic rather than a quarantine service. A less absolute prohibition was prescribed in 1555 on ships from Bordeaux and other French ports where plague was epidemic. The arrival of those vessels was reported to the magistrates of Edinburgh and they were then examined by town's officers. If there were no sick on board, no history of sickness or deaths during the voyage and no other suspicious circumstances the cargo might be landed, but only on condition that its owners agreed that if disease resulted they should be put to death and their goods confiscated!<sup>3</sup> The idea that epidemics might be prevented by threatening death to those who might be supposed to have spread the infection bulks pretty largely in early

public health legislation. Fortunately, it was not long before more efficient and less barbarous methods were devised.

Those varied in detail from time to time, but in broad outline remained pretty stable. When it became known that plague had broken out in any of the ports frequented by Scottish merchantmen proclamation was made at the market cross of Edinburgh, the pier and shore of Leith, and other places concerned, forbidding shipmasters from the suspected places to set any passengers or goods ashore until they had reported to the local authority who had to make a thorough examination and decide whether those on board were and had been "free from all infection or suspicion of sickness." The state of the plague at the port the ship sailed from and the nature of her cargo were also investigated. If all were satisfactory crew and passengers were allowed to come ashore and land their goods.

If, on the other hand, there were grounds for alarm—as, for instance, when a ship from an infected place reported sickness or deaths during her voyage—severe restrictions were imposed. Attempts to land were punishable by death. Ship, passengers and cargo underwent a very thorough process of disinfection, and an order of the Privy Council, dated 23rd September 1564, gives a good idea of how this was carried out. The cargoes of the ships concerned on this occasion consisted of lint, pitch, tar, iron, timber and barrels of potash, and, of course, the personal effects of passengers and crew. The order provides that :—

"because maist danger appearis to be amang the lynt, that the same be loissit and housit in St Colm's Inche, oppynit, handillit and cassin furth to the wynd every uther fair day quhill the feist of Martimes nixtocum be sic visitouris and clengearis as sall be appointit and depute thairto be the Provost, Baillies and Counsall of the burgh of Edinburgh upoun the expensis of the marchantis, awneris of the saidis guidis. And as consarning the uther Guidis pik, tar, irne, tymmer, that the samyn be clengit be owirflowing of the sey, at ane or twa tydis, the barrellis of asse to be singit with hadder set on fyre and that the schippis be borit and the sey watter to haif interes into thame to the owirloft, and all the partis within to be weschin and clengit ; and sic like that the marinaris and utheris that sall losse and handill the guidis abone written be clengit and kepit apart be thameselffis for ane tyme at the discretioun of the saidis visitouris, and license to be requirit, had and obtenit of the saidis Provest, Baillies and Counsall before thai presume to resort opinlie or quietlie amangis oure Soverane Ladies fre liegis." 4

The instruction that the lint should be "opened, handled and cast forth to the wind" refers to a process intended to serve both as a means of disinfection and a test of its efficacy. It must be remembered that the contagion of plague was believed to be a venomous quality in the air which penetrated and adhered to materials to an extent depending on their porosity and their liability to putrefaction. The

destruction of this atmospheric poison or its replacement by clean air was the object of disinfection, or—to use an old word perhaps more appropriate in this connection—"expurgation." Dry and moist heat were used, fumigation with a variety of odoriferous substances was recommended, but free ventilation was regarded as of high importance, and was the method of choice when dealing with infected textiles. It entailed opening up bags and bales, unfolding, shaking, beating and generally handling the contents for a number of days. It was supposed to be most effective in winter when the goods could be exposed to "aire of frost." The principle had been approved by medical writers on plague—Marsilius Ficinus, Mercurialis, Diemerbroeck and many others—and it was still one of the chief means of dealing with infected goods in the great lazaretto of Venice at the end of the eighteenth century.<sup>5</sup>

It was assumed that if the goods were really dangerous this would be demonstrated by some of the handlers developing plague. Hence the process is sometimes referred to as "taking the sey" (the assay or trial) "of the geir." Frequently the owners and their families had to do the handling themselves, the idea, no doubt, being that if anyone were to contract the disease it should, in justice, be the owner of the infected fomites.

The other methods of disinfection mentioned in the order—immersion in sea water for several tides, or singeing with burning heather—are examples of the "cleinging by fyre and wattir" often mentioned in official documents of the time. (Incidentally, flaming walls with burning heather was the approved method of disinfecting houses. It occasionally resulted in the house being set on fire—indeed, the whole town of Kelso was destroyed in this way in 1645.)

Clothing was boiled or heated in a kiln. What could not be dealt with in any other way was scrubbed, sometimes, it seems, with a good deal more vigour than discretion!

The most drastic method of disinfection was that applied to the ships themselves. They were "bored" and scuttled in tidal waters till their upper decks were awash—an effective method, no doubt, of destroying infected rats and fleas. After the ships had been raised again they were thoroughly cleaned. Finally all who had taken part in those various operations were isolated for a period that apparently might be varied at the discretion of the authorities.

The story of one unfortunate ship's company gives a fair idea of how the system worked. About the middle of September 1580 the *William*, owned and commanded by John Downey, arrived in the Forth from Dantzic.<sup>6</sup> There had been several deaths on board during the voyage. She was ordered to Inchcolm where her company—seventeen sailors and fifteen passengers—were to remain on pain of death, till they were "clengit of the said seikness." The authorities of all seaport towns were warned that if any of the *William's* people tried to land, or had landed already, they must be arrested along with

those who had received them—"thair houssis to be closit up and thameselvis to be execute incontinent to the deid." In fact, the authorities, as often happened, were content with a much lighter penalty than the law prescribed. A man named James Henry, with several companions, did succeed in leaving the *William* and arrived in Edinburgh. They were arrested there, but the magistrates, instead of hanging them "incontinent" as they were authorised to do, merely isolated them in their lodging. It is to be regretted that they showed no proper appreciation of this leniency. Baillie William Little, under whose supervision they had been placed, received so much insolence and abuse from them that as soon as their quarantine was over they were summoned to appear before the indignant town council, there to ask pardon of God and the baillie, and to admit that, so far as the latter was concerned, they had slandered him. In addition, they were fined £3 apiece.<sup>7</sup> (Baillie Little, by the way, was quite an important public man who became Provost of Edinburgh a few years later. What is perhaps of greater interest to us is that he was the brother and executor of Mr Clement Little, whose bequest of books to the town formed the nucleus of the University Library.)

In the meantime a number of "clengeris" had been sent to Inchcolm. Those were officers, both men and women, who were employed for various sanitary duties during outbreaks of plague, but mainly, as their name implies, for disinfecting persons and goods. Though employed by the municipality they had to be paid by the people requiring their services, an arrangement which, however commendable from the town council's point of view, would undoubtedly evoke vociferous protests from the modern rate payer! On this occasion relatives of some of the people who had already died at Inchcolm did protest, but without avail.

To complicate matters, news came from Flanders that the plague was "vehement" there, and on the 3rd October the *Wynden* arrived from Bruges, an infected town. She had some soldiers on board and also three pregnant women. They were isolated at Newhaven—probably the authorities had to recognise that huts on Inchcolm at the beginning of winter were not suitable accommodation for expectant mothers. The soldiers were allowed the same privilege, but other passengers apparently had to find surety for £100 apiece if they wished to be quarantined there.

At the same time a "fly-boat" arrived from Dantzic. Evidence of the care with which the authorities were making their enquiries is the fact that they discovered that she had on board three chests, with some other baggage and clothing, that had been transferred to her from the *William*. In view of that vessel's subsequent history the owners of this gear were given the choice of taking it to Newhaven and handling it there for 15 days, or sending it to be dealt with by the clengeris at Inchcolm—"and gif thai will nocht be content thairwith the said guidis and kystis to be brynt and destroyit."<sup>8</sup> Eventually,

however, the owner of one of the "kysts," was allowed to send it to his home in Peebles to be "handled" there, but only on condition that he left the key in Edinburgh. It was to be restored to him when he produced a certificate that his chest had arrived at Peebles and was under supervision by the magistrates of that town.

An entry in the Privy Council's register dated 22nd November indicates that things were going badly with the survivors of the *William*. They had now been confined on Inchcolm for nine weeks, Downey the skipper and a number of others were dead, the ship was leaking and likely to deteriorate badly, and the owners were at law with the merchants to whom the cargo belonged. The Town Council of Edinburgh were instructed to enquire into all the circumstances and thereafter to "tak sic order thairanent as thai sall think masist meet." But it was not until the middle of January, when the *William's* quarantine had lasted 115 days, that the last of the surviving sailors and passengers were released, the maistrates having decided that the danger of infection was over—"prayset be God"—a pious exclamation doubtless echoed by all concerned!<sup>9</sup>

The Council sometimes managed to get information about suspected ships before they arrived at Scots ports. In 1625 the plague was specially severe in London and other parts of England and a rumour reached Edinburgh that an infected ship had caused an outbreak at Holy Island, on the coast of Northumberland, and at Berwick on Tweed. Instead of asking the English authorities for confirmation of this the Council wrote to the Laird of Ayton in Berwickshire—"being ane gentleman of honour and credite who in our opinion is most able to gif unto us a true light and information of all the particulars concurring in this business." He was asked to report whence the ship came and what cargo she had brought, how long she stayed at Holy Island and where she went afterwards, what merchants traded with her, whether infection had been reported on either side of the border, and, finally anything else he might think of interest.<sup>10</sup>

The laird's reply is not available, but he seems to have investigated the matter thoroughly, as the Privy Council were fully informed about the suspected vessel when she appeared in the Forth shortly after. She had arrived at Holy Island from an infected port, but her captain had concealed that fact. When plague broke out and detection became imminent he fled to Norway. The Scots authorities were presumably not specially interested in his behaviour south of the border, and his misdemeanours would probably have been overlooked if he had been able to produce evidence of the good health of his crew since leaving Holy Isle. Being unable to do this he was ordered to leave the Forth at once and warned that if he or any of his crew attempted to land or to put goods ashore anywhere in Scotland they would be hanged.<sup>11</sup>

The long detention to which suspected ships were liable, the close confinement of passengers and crew in roughly improvised accommodation, often on barren islands devoid of all amenities, the expense, the

loss of market and the deterioration of goods that were the inevitable result of the quarantine system naturally resulted in many attempts to evade the regulations. A minute of the Privy Council dated 1st August 1625 refers to "a daylie and frequent arrayval of shippis and barkis from London." These, if not prevented, landed goods and passengers openly. If resisted they sent them ashore by boat at "obscure pairtis and burnis alongis the coast"—"the skippers pretending misknowledge of the saidis proclamations." The Council re-enacted their previous regulations, and, as evidence that they were in earnest, gave orders, when a ship from London came into Prestonpans a fortnight later, that an armed guard should be set over her, and that if any of her people attempted to land they should be killed at once "with shoittis of muskettis or haquebuttis or by pikis and halbertis." <sup>12</sup>

Attempts to disobey or evade the quarantine regulations were not confined to recalcitrant shipmasters: the magistrates of the coast towns also occasionally proved untrustworthy and disobedient. A flagrant case occurred in 1625 when David Robertson, a skipper of Leith, arrived from Dantzic with cases of plague aboard his ship. He was instructed to discharge his cargo at Inchcolm, where it would be dealt with, and then take the ship to Inverkeithing to be temporarily scuttled in the harbour there.<sup>13</sup> The baillies of Inverkeithing, however, "oppoised thameselffis be force and violence against the lying of the said ship in thair harborie," and, along with a local magnate who had encouraged them, were summoned before the Privy Council to answer for their misconduct—an experience which, three years later, was shared by the civic fathers of most of the Fifeshire seaports, all of whom were charged with having been "most remise and negligent in the execution and careful advertance to that whiche was given thame in charge." <sup>14</sup>

A case of some interest was that of the ship *Good Fortune* which, during 1627 arrived at Leith from London with a history of sickness and deaths during her voyage. After a good deal of ordering and counter ordering she was eventually quarantined at Alloa, where she had gone to take in a cargo of coals. The special feature in her case is that after twenty-three days detention she was released after a medical examination of her crew. Laurence Cokeburn, "chirurgion in Edinburgh," who certified her free from infection reported that he visited "the haill companie of the same, and speciallie one of the companie that had a byle upon him, whom he found sound and weele." <sup>15</sup> This is probably the first record of a medical man acting as port medical officer in Scotland. Cokeburn was the son-in-law of James Henrysoun, who is sometimes described as the first medical officer of health of Edinburgh. It is possible that on this occasion he may have been deputising for his father-in-law.

Towards the end of 1635 plague broke out seriously in the Netherlands, and a small epidemic at Cramond was ascribed to infection brought by Dutch ships. The usual regulations were put into force,



and amongst the shipmen who immediately got into trouble was a captain called William Moodie. The charge against him was, that having come from the Low Countries

"—where he knew that the contagious sickness of the pest was most violent, he verie unchristianelie, after he came in this firth, sett ashore at Werdie one callit Lyll, who was sicke for the time within the said ship and his sicknesse knowen to the haill equippage." Moodie protested his innocence but was convicted on the evidence of his own crew. He was imprisoned and kept in the stocks for a month, and then given the choice of returning to Holland or remaining in gaol. His decision is not recorded, but it must be allowed that he got off fairly easily.<sup>16</sup>

In fact, it is remarkable that, so far as can be ascertained, the extreme penalties threatened against those who disobeyed the ordinances concerning quarantine were never enforced. The mild, almost paternal, chastisement inflicted on these maritime transgressors is in strong contrast to that sometimes meted out to ordinary citizens, as, for example, during the epidemic of 1530, when the magistrates of Edinburgh hanged a man, drowned two women and banished or branded more than a dozen other persons, mostly for failing to notify cases of plague.

By the middle of the seventeenth century plague had disappeared from Scotland, but the risk of its re-introduction from less fortunate countries still worried the authorities. In 1661 "the Black Plague" was raging at Dantzic, and some infection referred to as "the new white plague" was spreading in Holland.<sup>17</sup> Once more quarantine was imposed on all ships reaching Scottish ports. But it seems that by this time the advisability of refraining from unnecessary interference with trade was becoming a little better recognised. Some distinction seems to have been drawn between cargoes that were thought specially likely to spread infection and those that were innocuous. Some consideration was given to the length of time a vessel had been at sea, and frequent references to "the ordinary tryall of fourtie days" suggest that quarantine no longer implied an indefinite period of incarceration. Nevertheless, it continued to be oppressive enough and attempts at evasion naturally continued.

In 1664 reports about the epidemic in Holland became so alarming that it was decided to stop the Dutch trade entirely. Very drastic regulations were made, but unfortunately their administration had to be left to a large number of authorities, "—magistratts of burghes, shireffs of shires, stewarts of stewartries, baylies of regalities, justices of peace, barrones and heritours."<sup>18</sup> Overlapping and confusion were inevitable, and ample opportunities for evasion were available to intelligent and unprincipled mariners. Some Dutch ships for example, defied the authorities at Bo'ness, and the Duke of Hamilton's agent was empowered to burn them if they did not put to sea at once. They did so, but one, at least, slipped back and attempted to take in a cargo

of coal. This was stopped by the agent getting sanction to burn her wherever he could catch her above Queensferry, unless she left immediately—which, apparently, she did.

But a complete ban on the movements of shipping could not be enforced. Scots shipmasters, faced by the prospect of remaining tied up in Dutch harbours till seized for debt, often preferred to take the risk of running for home, and the Privy Council had to recognise that the policy of threatening to hang mariners and burn their ships had its limitations. The regulations were relaxed in several cases, the Council apparently dealing with each on its merits. But some got pretty severe treatment. David Thomson, for example, obediently remained in Holland till his ship was on the point of being seized. He then set sail for Scotland, but, caught in a winter storm, was driven right round Britain. On 10th November he reports that he and his company are "by God's mercy arryved at Greinok fyftein dayes since." All on board are in good health, but they are forbidden to come ashore. Their ship is damaged, they are in hazard of their lives, and they crave the Council's permission to land with their goods. It is now forty-five days since they left Holland.

The ship had a mixed cargo, parts of which may have been considered dangerous, and it was possibly for this reason that the Council insisted on the crew being isolated at Greenock for the customary forty days—at their own expense, of course—and directed that any of the goods that could not be properly disinfected must be burned.<sup>19</sup>

The Great Plague of London broke out in the following year. All trade between London and Scotland was interdicted, and the authorities hastened to make preparation for the epidemic that might be expected if the infection spread northward. But nothing untoward happened. Not until October did any suspicion of sea-borne infection arise, when three ships were sent to Inchkeith to be detained there for the usual forty days. They were released in due course, the authorities being convinced that there was no danger of infection. London was free of plague by the end of the following year; within a few more years the disease had ceased to be a serious problem in Western Europe, and with the disappearance of a menace that had lasted for more than three centuries the record of the Scots quarantine service comes to an end.

It is difficult to say how far it served its purpose. In conception it was sound enough. We are not justified in demanding from any activity of preventive medicine more than that it shall be based on the best medical knowledge of the age, and that the best means available shall be used for the practical application of that knowledge. So regarded, the preventive measures devised by the civil authorities were, for the most part, quite reasonable. The doctrines on which they were based were those held by all the orthodox physicians of the time—that infection was caused by an aerial poison, and that disease

acquired thereby might be spread by contagion. We have discarded both the theory of infectious miasmata and that of "contingent contagion," but it is well to remember that they survived, as fundamental tenets of epidemiology, till well into the nineteenth century. In light of those beliefs the lengthy quarantine imposed and the methods of disinfection used were logical enough. It is, perhaps, not irrelevant to point out that when, a few years ago, it seemed possible that we ourselves might be exposed to an aerial poison with qualities rather similar to those of the hypothetical plague venom—I mean mustard gas—we proposed to use methods of decontamination that would have appeared quite obvious and perfectly familiar to anyone who had had experience in dealing with plague four hundred years ago.

The real weakness lay less in the theory than in its practical application. Lack of any permanent machinery for dealing with epidemics, the number of small local authorities attempting, within restricted areas, to carry out duties for which they had inadequate resources and little enthusiasm, and, not least, the primitive means of transport and communication—services on which efficient administration largely depends—all militated against success.

Several outbreaks of plague in Scotland—in particular that which lasted from 1584 till 1588—were attributed, at the time, to infection from overseas, but no evidence is now available for determining whether the attribution was justified. It may well be that endemic centres in this country in which the plague was always smouldering were a more pressing danger. Nor is it possible to say how far the quarantine regulations I have outlined afforded a real protection. It is easy to point out that maritime quarantine has never been an absolute safeguard, that it must entail much hardship and dislocation of trade, and that the present system of medical inspection and supervision gives much better results. But that system has become practicable only because we now possess the very facilities which in former days were conspicuously absent—a permanent administrative machine with close communication and co-operation between its units. Lacking this, our forefathers did their best with what they had. Whether the protection they improvised was of real value or not its story may have some interest as dealing with one phase in the evolution of our health service, and as showing how men, with limited knowledge but with courage and public spirit, faced the recurring menace of one of the most terrible epidemic diseases.

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## NEW BOOKS

*A Handbook for Nursery Nurses.* By A. B. MEERING, S.R.N. Pp. xi+509, with 118 illustrations. London: Baillière, Tindall & Cox. 1947. Price 17s. 6d.

This book has been planned to cover the syllabus of the certificate of the National Nursing Board. It deals with elementary anatomy and physiology, with nutrition, growth and hygiene, with simple ailments, defects, accidents, infections and fevers and there is a section on home nursing. Infant feeding and cooking for children receive full attention and the care and management of the child at different stages is described in detail.

The book is written in clear and simple language; it is full of helpful and practical information and it should be of interest not only to the nurse but also to any woman who has the care of young children.

*Bone and Bones, Fundamentals of Bone Biology.* By JOSEPH P. WEINEMANN, M.D., and HARRY SICHER, M.D. Pp. 464, with 289 illustrations. London: Henry Kimpton. 1947. Price 50s. net.

This book is the combined effort of a pathologist and an anatomist, both associated with the School of Dentistry of the Loyola University of Chicago. The reason for the somewhat peculiar title is explained in the Introduction—"bone" being regarded as a tissue, whilst "bones" are considered as organs. The first two chapters, forming Part I, are devoted to the normal structure and growth (*a*) of osseous tissue, and (*b*) of types of bones. In the latter, periosteum is studied; whilst in the former only the cells of the tissue "bone" are dealt with.

Part II has nine chapters devoted to the pathology of bone and bones. Developmental disturbances and deformities of the skeleton are dealt with in general, and in relation to particular examples, *e.g.* Achondroplasia. Then follow three chapters dealing with effects of endocrines, vitamins and minerals in osseous pathology. Healing of bones takes a chapter and then there follow, under the heading of necrosis and inflammation of bones, in addition to what is usually included under such a heading, Hand-Schüller-Christian's disease, Gaucher's and Niemann-Pick's diseases.

In the chapter devoted to tumours of the skeleton, no mention of Adamantinoma is made, though earlier, considerable space is devoted to the development and certain changes in teeth. In this chapter a short note is given of "senile hyperostosis of the skull," but in the references the name of F. Henschen of Stockholm, who has published extensively on this, does not appear. There are what might be regarded as some other omissions, *e.g.* developmental suppressions or fusions of bone, but, as a whole, this book is informative and at times provocative, perhaps—as explained in the preface—"intended to be a challenge to the research worker." It gives detailed accounts of the basic features of the biology of bone—and bones, and it gives briefer accounts of the many pathological changes. It is well illustrated, has a good list of references, and a detailed index.

*Laboratory Manual of Anatomy and Physiology.* By NELLIE D. MILLARD, R.N., B.S., M.A., and MARY JANE C. SHOWERS, R.N., B.S. Pp. viii+119, illustrated. London: W. B. Saunders Co. Ltd. 1946. Price 5s.

This manual, by two instructors in American schools of nursing, contains practical exercises arranged in thirty two-hour lessons designed to supplement text-book study. Many comments could be made on individual items; but it is sufficient to say that perusal of the exercises and the directions to the student-nurse to summarise each gives the impression that this is "potted" anatomy and physiology. The question is whether this type of instruction is really necessary or effective in the education of nurses.

## NEW EDITIONS

*The Care of Tuberculosis in the Home.* By JAMES MAXWELL. Second Edition. Pp. 112. London: Hodder & Stoughton Ltd. 1947. Price 7s. 6d. net.

This little book is designed to help the tuberculous patient in his efforts towards recovery. It is written simply and lucidly and its seventeen chapters contain a great deal of useful information. The rationale of the stages and forms of treatment is explained in a way which cannot but be helpful to the patient and to the family doctor who has to supervise the régime.

*An Introduction to Medical Statistics.* By HILDA M. WOODS and WILLIAM T. RUSSELL. Second Edition. Pp. x+125. London: Staples Press. 1945. Price 8s. 6d.

Recognising that most recent graduates in medicine have little more than an elementary knowledge of arithmetic and algebra, the authors have written this little book to explain the mathematical processes necessary in public health work. The book is limited in scope but will admirably serve the purpose for which it is intended.

*Elements of Surgical Diagnosis.* By A. P. GOULD. Ninth Edition, revised by Sir CECIL WAKELEY, K.B.E., F.R.C.S. Pp. xv+718, with 22 illustrations. London: Cassell & Co. Ltd. 1947. Price 15s. net.

This book is intended for the pocket of the student working in a surgical ward. Its purpose is to indicate firstly how to examine a patient and secondly, by listing the conditions which may occur in a certain region, to lead one to a diagnosis. For immediate reference it is excellent.

*A Textbook of Clinical Neurology.* By ISRAEL S. WECHSLER, M.D. Sixth Edition. Pp. xv+829, with 162 illustrations. London: W. B. Saunders Co. Ltd. 1947. Price 42s.

This textbook continues to enjoy popularity after nearly a quarter of a century, as indeed it merits from its original intention of serving the medical student and family practitioner. Clear in style and terse, it emphasises in every page the vast knowledge and experience of the author. The psychological approach is especially valuable in these days when the modern tendency is too often towards an unimaginative stereotyping of different clinical entities.

The introduction of a skilful chapter dealing with neurosis in a textbook of this nature is significant, and seems to emphasise the desirability of bridging the gap between neurology and psychiatry, yet, in doing this service the author does not omit the recent advances in therapy which are mostly concerned with the organic aspects of his subject. References are concise and excellent, being well chosen and providing a splendid guide to more detailed information in the respective fields.

This book seems to fill a lack in the numerous other works obtainable in Britain, none of which have quite the same approach to the subject, and perhaps it scores in these days by its obviously unaustere format.

*Demonstrations of Physical Signs in Clinical Surgery, Part I.* By HAMILTON BAILEY, F.R.C.S. Eleventh Edition. Pp. xi+100, with 178 illustrations. Bristol: John Wright & Sons. 1948. Price 8s. 6d. per part.

The author explains in his preface that publication of a new edition has been held up by shortage of paper and labour and he has been forced to hasten its appearance by issuing the book in paper-covered parts.

Considerable revision of the text has been carried out and there are many new illustrations. This should enhance the value of an already useful and popular work.

*Emergency Surgery*, Part II. By HAMILTON BAILEY, F.R.C.S. Sixth Edition.  
About 1000 pp., illustrated in colour. Price 21s. per part.

The second paper-bound part of *Emergency Surgery* is devoted to the surgery of the acute abdomen, and maintains the same standard of graphic usefulness as the first. It is profusely illustrated, and those figures showing the steps of the various operations will be particularly helpful to the young surgeon.

## BOOKS RECEIVED

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# Edinburgh Medical Journal

December 1948

## PNEUMONIA—A SURVEY—PAST AND PRESENT

By THOMAS ANDERSON, M.D., F.R.F.P.S., F.R.C.P.E.

It is now commonplace to say that there has been a complete alteration in the severity of the acute infections during the past twenty years. In Glasgow, for example, when the period 1920-23 is compared with the period 1944-47, we find that the mortality from the common infectious diseases \* has fallen from a total of 4725 to a total of 516 deaths. Pneumonia has, of course, shared in this improvement, although it is probably true to say that the reduction is less (Table I).

TABLE I

*Mortality in Glasgow from Various Infectious Diseases*  
1920-1923 : 1944-1947

Disease.	1920-23.	1944-47.
Measles . . . . .	2267 (100)	79 (3.5)
Scarlet Fever . . . . .	260 (100)	17 (6.7)
Whooping Cough . . . . .	1404 (100)	168 (11.8)
Diphtheria . . . . .	573 (100)	145 (25.4)
Cerebro-Spinal Fever . . . . .	221 (100)	107 (48.4)
Total . . . . .	4725 (100)	516 (10.9)
Pneumonia . . . . .	6898 (100)	2729 (39.6)

Such a direct comparison of the beginning and end of a twenty-eight year period makes it rather easy to infer that the change is a direct result of the introduction of modern methods of chemotherapy. But we need to be reminded that the reduction has been continuous throughout the whole period: and that for all the diseases, improvement had already occurred prior to the introduction of the sulphonamides in 1936. Such periodic changes in the behaviour of the acute infections have of course been a feature of their history. Unlike the degenerations and metabolic disorders which are the interest of the general physician, the acute infectious diseases are constantly in a state of change as they reflect alterations in the relationship between host and parasite.

A Honyman Gillespie Lecture delivered in the Royal Infirmary, 25th November 1948.

\* Scarlet fever, diphtheria, measles, whooping cough and cerebro-spinal fever.



Because of the accelerated life-cycle of the parasite we may assume that changes in its attacking power can occur relatively quickly in time: and in the past the fluctuations in the severity of an infection have usually been ascribed almost solely to alterations in the "virulence" of the attacking agent. But the clinical pattern of an infectious disease must always be the resultant of two forces—host and parasite; when alterations occur we must be prepared to study both. Changes in the parasite have received more attention in the past mainly because they lend themselves more easily to study; but, even if our knowledge is still incomplete, consideration of the response of the host is important. Accordingly those aspects of our knowledge of pneumonia which reflect this host-parasite relationship have been chosen for study in the present paper.

There is no doubt that the first interesting feature in regard to the host-parasite relationship of pneumonia is the realisation that, although at all ages the pneumococcus is responsible for the bulk of the infections, the *spectrum*, as it were, of pneumococcus types varies at different ages. Now pneumonia is not alone in being an infection caused by a pathogen divisible into a number of serological types. But, in all the other infections variations in the distribution of the different types can be related to such factors as season, year or place. There is no suggestion, for example in diphtheria, that there is any difference in the distribution of the three main types in respect of different ages; nor is there any evidence that scarlet fever is caused by different types of streptococcus at different ages. In pneumonia, however, it is well known that the pattern of the types of pneumococci which cause the disease in infancy is different from that in later childhood. As age advances further into the middle-age groups the distribution of types becomes more stable, until again in the later ages there is a return

TABLE II

*Bacteriology of 71 Cases of Pneumonia in Childhood*

Type VI	.	.	.	.	.	11 (15.5 per cent.)
XIX	.	.	.	.	.	11 (15.5 „ )
XIV	.	.	.	.	.	10 (14.0 „ )
I	.	.	.	.	.	5 ( 7.0 „ )
Str. hæmolyticus	.	.	.	.	.	5 ( 7.0 „ )
Pn. (untypable)	.	.	.	.	.	4 ( 5.6 „ )
Types II, III, XXIII	.	.	.	.	.	3 each
Types XII, XIII, XVIII, XX, XXI	.	.	.	.	.	2 each
Types IX, X, XVI, XXIX, XXXI	.	.	.	.	.	1 each
str. viridans						

*N.B.*—From two cases were obtained two types—namely I and VI and I and XVI—these are listed under Type I.

to the more chequered pattern seen in the earlier age groups. The results of the typing of pneumococci from a group of children with pneumonia are shown in Table II and certain details of the distribution

are depicted in Figs. 1 and 2. These may be contrasted with the results of typing in adult pneumonia where types I to VIII account for 85 per

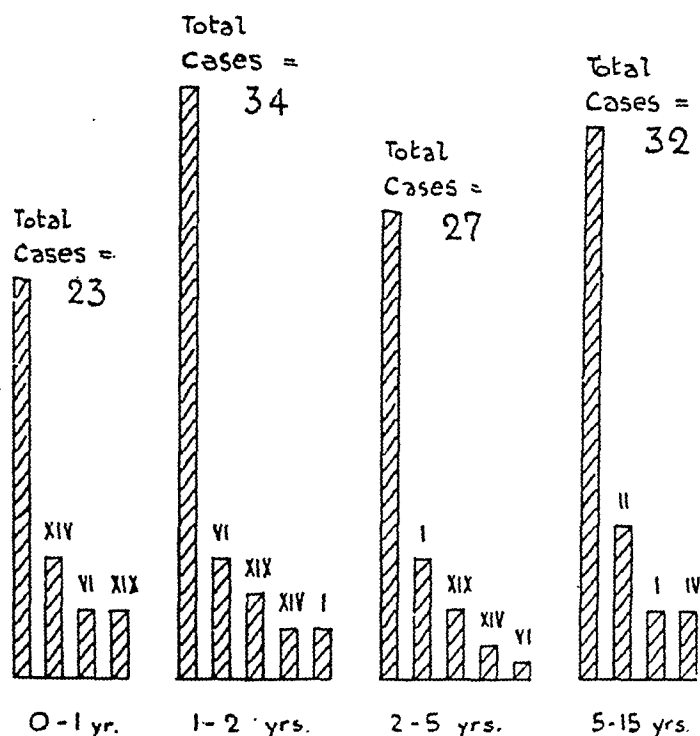


FIG. 1.—Distribution of pneumococcal types in 116 cases of pneumonia. Aged 0-15 yrs.

Age-distribution of common types, 0-6 years  
(throat swabs & purulent complications combd)

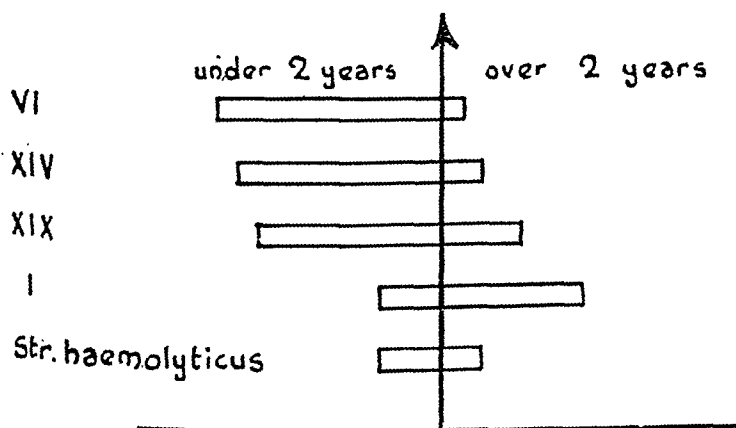


FIG. 2.

cent. of the cases. It may be seen at once that the pattern is entirely different. But not only is the difference apparent as between children

and adults ; when the figures for the first five years of life are divided into their different age groups we find that as infancy gives way to childhood so the distribution of the types causing pneumonia begins to conform to that seen in the adult. Then as we advance past middle life we find that the causative types change so that type III and higher types become more prominent (Table III).

TABLE III

*Age Distribution of 714 Cases of Adult Pneumonia due to  
Pneumococcus Type I, II and III*

	Type I.	Type II.	Type III.	Total.
15-40 . . . . .	182 (39)	254 (55)	28 (6)	464 (100)
41+ . . . . .	60 (24)	142 (57)	48 (19)	250 (100)
Totals . . . . .	242	396	76	714

The figures in brackets are percentages of the line total.

Although this alteration in type distribution with age is well known, it forms a basis for suggesting a profound difference in the host-parasite relationship at different ages. It is reasonable to argue that the age distribution of an infectious disease must reflect the extent to which the population is subjected to contact with the causative organism. When the child population is predominantly attacked it may be assumed that the organism is highly prevalent in the community and that it is one of the conditions of growth that the host comes to terms with it at an early age. In such an event we may find that the organism is fairly frequently carried by healthy adults—who have developed immunity by infection in childhood ; but, if so, we shall expect the distribution of types carried by adults to be similar to that found in cases in childhood. This is true, of course, for pneumonia in infancy and early childhood where the types found are similar to those carried by healthy adults. Pneumonia in childhood may thus be pictured as an endemic infection occurring in a population as a result of exposure to organisms commonly present in the nasopharyngeal flora of normal persons.

When pneumonia in the adult is considered we find that the types responsible are not those commonly found either in normal throats or in the sputum from persons suffering from chronic bronchitis or pulmonary congestion (see Table IV). Pneumococci of types I and II are isolated almost solely from patients with pneumonia or from their close contacts. The adult population has presumably acquired some basic resistance to the higher types as a result of infection in infancy and is only successfully invaded by organisms which possess additional attacking powers.

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## PRE-NATAL DIET

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- Vitamin E The fertility or anti-sterility vitamin.
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Such a rationalisation of the problem possibly over-simplifies the picture but it suggests that two deductions may be drawn. In the first place it is perhaps unwise to think of pneumonia as a single

TABLE IV

*Type of Pneumococcus Isolated from 55 Patients  
Bronchitis, etc.*

Type III	.	.	.	.	.	.	.	.	14 (25.5)
" VIII	.	.	.	.	.	.	.	.	9 (16.4)
" XVI	.	.	.	.	.	.	.	.	5 (9.1)
" VI	.	.	.	.	.	.	.	.	4 (7.2)
" XI	.	.	.	.	.	.	.	.	3 (5.4)
" XIII	.	.	.	.	.	.	.	.	3 (5.4)
" IX, X, XXVII, XXI	.	.	.	.	.	.	.	.	2 each (3.6)
" II, XVII, XVIII, XX, XXIII, XXXII	.	.	.	.	.	.	.	.	1 each (1.8)
No pneumococcus	.	.	.	.	.	.	.	.	3 (5.4)

infectious disease occurring in persons of all ages but almost as a combination of two disease-patterns superimposed on each other. The first is the pulmonary infection due to the "commensal" types and shows an age-distribution similar to that of such prevalent infections as measles and whooping cough. (The term "pulmonary infection" is used because it is probably correct to assume that actual pneumonia in childhood is but the more obvious manifestation of an infectious disease which includes all varieties of milder respiratory tract infection.) The second is a disease due to less common (but more invasive) types of pneumococci to which man may have been exposed more recently in time; exposure is here more likely to arise from the extra-domiciliary contacts of adults at their work and in their travel to and from it. But since only a small proportion of the population exposed is successfully attacked infection demands not only a greater invasiveness on the part of the organism but some temporary weakening of the host's resistance.

This view in turn emphasises a broad distinction between pneumonia in the adult and in the child; the former has acquired some basic experience of the pneumococcal family and is normally resistant to infection, whereas the latter is a susceptible host whose experience of the organism is slight. It may, therefore, not be surprising to find that the benefits of chemotherapy are more obvious in the adult, for, once the organism has been shorn of some of its attacking capacity by sulphonamide or penicillin the host can soon assert his ability to withstand it. The figures for the mortality in Glasgow from pneumonia leave one in little doubt that the disease still causes death in a disproportionately high number of children in the first year of life (Table V).

It is not desirable to make dogmatic inferences from the figures in Table V, but it is interesting to observe that in the last twenty-eight years the fall in mortality during the first year of life from whooping

cough more closely resembles that of adult pneumonia than that of pneumonia in the first year of life; and one is tempted to deduce that, in infancy, pneumonia is not so much an acquired, exogenous

TABLE V

*Comparison of the Number of Deaths from Whooping Cough and Pneumonia at Different Ages*

1920-1947

Period.	Whooping Cough 0-1 Years.	Pneumonia.	
		0-1 Years.	1-45 Years.
1920-23	583 (100)	2026 (100)	2987 (100)
1924-27	773 (132)	2183 (108)	2942 (98)
1928-31	599 (103)	2113 (104)	3074 (103)
1932-35	366 (63)	2160 (107)	2177 (73)
1936-39	308 (53)	1664 (82)	1540 (52)
1940-43	218 (37)	1443 (71)	740 (25)
1944-47	93 (16)	984 (49)	380 (13)

infection of a healthy child (as, for example, in whooping cough) as an endogenous infection of a child whose capacity to withstand its own commensals has been previously reduced by some other factor.

But if one thus suggests that in a broad way the end of the first year of life represents a transition from a state of relatively high susceptibility to one of increasing resistance it is also possible to suggest that the age of 40 years constitutes a second climacteric when resistance again becomes impaired. For the study of this aspect of the question it is interesting to analyse the various factors which seem of importance in the occurrence of bacteraemia in adult pneumonia. Bacteraemia must always be a valuable criterion of the end-result of the host-parasite complex for it must indicate either an increase in the capacity of the organism to invade or a failure of the host's capacity to defend. In order to focus the enquiry as much as possible attention is directed to a group of 166 patients suffering from pneumonia due to pneumococcus type II which, in Glasgow, is the most frequent single causative organism in any series of adult patients. The concentration of attention upon one type is important in that it removes the possibility of any natural variations (perhaps unappreciated) between one type and another. The relevant figures are shown in Table VI. As many other investigators have observed, age emerges as a factor of great importance in deciding the occurrence of bacteraemia. Indeed a further table shows that those other factors which seem to be associated with a high bacteraemic rate are themselves intimately associated with age: for the duration of illness prior to admission and the extent of consolidation are both significantly correlated with age, a fact which might easily explain the slight (but statistically insignificant) increase in the bacteraemic rates in patients admitted late and with more

extensive consolidation (Table VII). It would seem that as age advances the patient tends to be admitted at a later stage of his illness

TABLE VI

*Examination of the Bacteriæmic Rates (per cent.) in Type II Pneumococcus Pneumonia in Respect of Certain Factors Thought to Influence it*

	Bacteriæmic.	Non-Bacteriæmic.	Total.	Bacteriæmic Rate Per Cent.	Standard Error.	S.E.D.* Diffce.
For the complete series . . .	56	110	166	33.7	±3.67	...
For Male cases . . .	43	75	118	36.5	±8.20	1.14
For Female cases . . .	13	35	48	27.1		
For cases 11-40 years . . .	26	73	99	26.3	±7.51	2.45
For cases 41 years and over . .	30	37	67	44.8		
For cases ill 3 days or less on admission	†30	70	100	30.0	±7.61	1.31
For cases ill 4 days and longer on admission	26	39	65	40.0		
For cases in which only one lobe was involved	†33	81	114	29.0	±8.16	1.86
For cases in which more than one lobe was involved	23	28	51	45.1		

\* S.E.D. = ratio  $\frac{\text{Standard Error of Difference}}{\text{Difference}}$ .

† = one case undefined.

TABLE VII

*An Examination of 164 Cases of Type II Pneumococcus Pneumonia*

The sex, duration, in days, of illness prior to admission, and the extent of consolidation in patients under and over 40 years of age

Age Group.	Male.	Female.	Both Sexes.	0-3 Days Ill Prior to Admission.	4 or more Days Ill Prior to Admission.	All Cases.	One Lobe Involved.	More than One Lobe Involved.	All Cases.
Under 40 yrs.	71 (70)	28 (29)	99	67 (59)	31 (39)	98	76 (68)	37 (45)	113
41 yrs. and over	47 (48)	20 (19)	67	32 (40)	34 (26)	66	22 (30)	29 (21)	51
All ages	118	48	166	99	65	164*	98	66	164*

(The figures in brackets represent the "expected" number which would have been noted had the cases in each sector been distributed by chance.)

\* 2 cases undefined.

with a more extensive consolidation. Such a finding is in accord with the clinical observation that the onset of the infection is less characteristic in the older patient; conditions primarily diagnosed as bronchitis only gradually emerge as true pneumonic consolidation so that it is often difficult to mark exactly the correct day of onset.



This study of bacteriæmia as an index of the host-parasite relationship in the individual can be further extended. As has already been observed, the fact that the mortality of many of the infectious diseases was falling consistently throughout the period prior to the introduction of sulphonamides and penicillin often induces the simple conclusion that the micro-organisms concerned were already losing their capacity to attack. Obviously the incidence of bacteriæmia at different periods of time in persons drawn from the same population should prove of some value in assessing the invasive power of the attacking organism. The removal of blood for culture on admission to hospital has been a routine procedure in the great majority of my cases of pneumonia over a period of many years. It is interesting to record therefore that in succeeding periods of time since 1939 the bacteriæmic rates have been 26, 18, 21 and 20 per cent. respectively. (These figures are shown in Table XI which records the results obtained with different methods of treatment.) These figures relate to a single blood culture performed on admission before starting specific treatment. It is not easy to compare these rates with similar rates prior to chemotherapy for two reasons. In the earlier period blood cultures were often examined on several occasions during the course of the illness so that some patients might have three, four or even more consecutive examinations. Such repeated examinations naturally increased the frequency of positive results so that the "bacteriæmic-rate" was higher and direct comparison with the present figures impossible. Further, there are obvious disadvantages in comparing the present rates with those obtained elsewhere (for example in America) for the comparison would then be vitiated by differences due to such factors as race, climate and social conditions. Fortunately Christie (who was responsible for some of the early work in Knightswood Hospital) has published figures for patients admitted from the same city districts and social class as those which comprise the present series. In considering his figures it is necessary to make allowance for the fact that he conducted repeated examinations; but his published figures have been recorded in such detail that it is possible, by a simple sum in proportion, to make an estimate of his rate for bacteriæmia on admission. Using such a method of estimation, we find that the rate for his cases, examined in 1933, was 28.3 ( $\pm 4.1$ ) per cent.—a figure very little higher than the rates obtained in more recent years. It is thus apparent that for patients admitted to the wards of Knightswood Hospital the incidence of bacteriæmia has altered very slightly during the last fifteen years.

But the existence of a bacteriæmia can be examined even more precisely. It is now a common practice to carry out a quantitative blood culture. This is done by adding 2 c.c. of the patient's blood to 15 c.c. of melted agar (which has been allowed to cool) and pouring the mixture into a Petri dish to form an ordinary blood-agar plate. If it is assumed that each subsequent colony appearing after incubation

has arisen from one single organism then an estimate can be obtained of the number of organisms present in one cubic centimetre of blood. Such an examination was made on 22 patients with bacteraemia by Christie in 1933 and in 95 patients during the period 1941-48 by various of my junior colleagues. The results of this examination are shown in Table VIII. It is interesting to find that the comparison permits

TABLE VIII

*Results of Colony-Counts in Pneumococcus*

## PNEUMONIA

(Result of first culture taken on admission)

Period.	Distribution of Number of Colonies per c.c.			Total.
	None.	-100.	100+.	
1933 . . .	8	12	2	22
1943-48 . . .	53	24	18	95
Total . . .	61	36	20	117

*Note.*—2 c.c. of blood, withdrawn aseptically, are added to melted agar and a pour-plate made in a Petri dish. After incubation for 24 hours at 37° C. the number of colonies observed in the plate are counted and this total divided by two gives an indication of the number of organisms present in 1.0 c.c. of blood.

of the same broad conclusion as was made from the study of the ordinary blood culture. There are obvious differences between the two groups of cases and a higher proportion of cases is now admitted with organisms present in 5.0 c.c. (*i.e.* in the ordinary broth culture) but absent from 2.0 c.c. of blood. Such a difference might be explained by surmising that some patients receive a small amount of sulphonamide at home which reduces the degree of infection; and it is intended to make further examination of this point in a subsequent publication. But it is equally clear that a considerable proportion of bacteraemic patients are still admitted with a heavy infection. Put in another way we may conclude that the pneumococcus has by no means lost its power of invasion; and that when invasion of the blood stream has occurred the capacity of the organism to flourish therein has not been reduced.

The importance of the quantitative blood culture gains additional emphasis when it is realised that in Christie's series, five out of seven patients with more than 30 colonies per c.c. died: in the present series, treated by sulphonamide or penicillin, there were 18 patients with more than 100 colonies per c.c. and only eight of them succumbed. Such impressive figures as these demonstrate the real efficacy of chemotherapy in pneumonia.

It has already been suggested that differences exist in the capacity of the various pneumococcal types to invade the tissues. In regard

to the occurrence of bacteriæmia with the individual types (Table IX) the differences are not always great in extent and indeed the rates for

TABLE IX

*Rates of Bacteriæmia with Different Pneumococcal Type*

	Pneumococcus Types.				Total.
	I.	II.	III.	Higher Types.	
Blood Cultures performed . .	49	166	42	110	367
Blood Cultures positive . .	11	56	12	17	96
Bacteriæmic rate per cent. . .	22·5	33·7	28·6	15·4	26·0

Combined rate types 1, 2 and 3 = 30·9 per cent.

types I, II and III do not differ significantly. But there is a significant difference between the combined rates for types I, II and III and the higher types. The ability of these latter types to invade the blood stream is clearly reduced. Such a finding is in keeping with the earlier suggestion that the adult has acquired some ability to withstand attack by them. But a further index of the pathogen's behaviour is the occurrence of complications presumably due to invasion. For the purpose of this examination the figures for empyema and meningitis occurring as complications of pneumonia may be scrutinised (Table X).

TABLE X

*Type of Pneumococcus in Invasive Complications of Pneumonia*

Type of Pneumococcus.	Empyema.	Meningitis.	Average Distribution of Pneumococcal Types in Pneumonia.
1 . . . . .	23 (30)	0	15
2 . . . . .	10 (13)	9	40
3 . . . . .	7 (9)	0	10
4-8 . . . . .	2 (2·6)	4	20
9-32 . . . . .	8 (10·6)	4	10
Untypable . . . . .	3	1	...
Str. pyogenes . . . . .	9 (12)	1	2
Anaerobic strep. . . . .	2	0	...
Str. viridans . . . . .	1	0	...
Staphylococcus . . . . .	9 (12)	0	less than 1
K. pneumoniae . . . . .	2	0	...
	76	19	

The figures in brackets are percentages.

In order to focus the comparison there is included in the table the rough percentage distribution of pneumonia patients during the period in which these cases were collected. It at once becomes clear that certain types of pneumococci contribute more and others less than

their share of the two complications. Thus type I is a common cause of empyema although it infrequently produces meningitis: but type II is less frequently encountered in empyema although it is the most common cause of meningitis. Whilst not immediately of interest it may be noted that *Str. pyogenes* and *Staphylococcus* (which are not responsible for a large proportion of cases) produce a high proportion of empyemas.

Now it is usual to describe the presence of pneumococci in the blood stream in pneumonia as a "bacteraemia." The use of such a term emphasises that the organisms reach the blood more as the overspill from a local lesion than as an actual invasion. The comparison of empyema and meningitis is thus interesting for these complications are, of course, more frequently observed in patients whose blood culture is positive: but whereas the former of these indicates a mere local invasion, the latter must represent a more virulent dissemination of bacteria. The contrast in the behaviour of the two organisms suggests that the term bacteraemia may be appropriate with type I infections; but for type II infections it might be more reasonable to use the term septicæmia.

Any final assessment of the host-parasite relationship must obviously rest upon the outcome of the infection. No doubt the quantity of the infecting dose must be taken into account but, even when we cannot ascribe a cause for the failure, death must indicate that in *this* struggle the host was unable to resist the invader. The introduction of chemotherapy does not materially alter such a conclusion; for it is worth while making the obvious statement that in chemotherapy it is the pathogen that is treated chemically, not the host. Even when the chemical successfully subjects the pathogen the host is still left with the task of arranging for its disposal; and, no less important, for the restoration of the damaged tissue to normal.

The initial success of sulphapyridine tended to induce the train of thought that we were now entering a period of better and better chemicals which would successively reduce the mortality from pneumonia. When a chemical is successfully applied in treatment it must indicate that its toxic effect upon the tissues of the host is more than counterbalanced by its lethal action on the bacterium. If the mode of action upon the pathogen remains constant a lessening of the toxic action upon the host will produce an apparent improvement in efficacy. But such an improvement will have a definite end-point; a stage will be reached when no more can be done by lessened host-toxicity to improve antibacterial effect—when further improvement must rest upon an enhancement of the host's capacity to dispose of the results of the infection.

Now sulphapyridine was undoubtedly a toxic drug. Those medical men who had to take it themselves made it abundantly clear to their colleagues that it was a question which was worse, the cure or the disease. Once this toxic effect was reduced by the introduction of newer

compounds, therefore, an improvement in mortality-rate could be expected. But with the appearance of such chemicals as sulphathiazole and sulphadiazine the toxic action on man was so reduced that very little further change in mortality could in fact be produced. It is true to say that most of the claims for the superiority of this or that sulphonamide depend little upon an observed reduction in mortality and more upon apparent reduction in toxicity. (In this respect it is difficult to understand the American distaste for sulphathiazole, which has, in my own experience at least, shown little difference from sulphadiazine in its toxic effects.)

But, even when it was reduced to a minimum, the toxic effect of sulphonamides was still quite a real thing. So that the introduction of penicillin, with its almost ideal freedom from toxicity, was the final *reductio ad absurdum*: here at last we should observe the pure effect of anti-bacterial therapy uncontaminated by any deleterious effect of the treatment upon the host.

In an attempt to view this reasoning objectively, the results of treatment over the past eight or ten years have been conjoined in Table XI. It should at first be made clear that at no time was treatment

TABLE XI

*Comparison of the Effects of Different Methods of Chemotherapy*

Method of Treatment.	Bacteriæmic Cases.		Non-bacteriæmic Cases.		Total Cases.	Total Deaths.
	Cases.	Deaths.	Cases.	Deaths.		
Sulphapyridine . . . .	59	16	165	13	224	29
Sulphathiazole and Sulphadiazine	51	11	239	10	290	21
Penicillin (intramuscular route)	27	8	99	4	126	12
Penicillin * (oral route) . .	17	4	67	1	84	5
Totals . . . .	154	39	570	28	724	67

\* Some of these cases received a single intramuscular injection at the start of treatment.

## SUMMARY

Treatment Group.	Incidence of Bacteriæmic in Group.	Fatality-rate in		Fatality-rate of Group.
		Bacteriæmic Cases.	Non-bacteriæmic Cases.	
Sulphapyridine . . . .	26.5	27.0	7.9	13.0
Sulphathiazole } . . .	17.6	21.5	4.2	7.2
Sulphadiazine }				
Penicillin (intramuscular) .	21.5	29.5	4.0	9.5
Penicillin (oral) . . . .	20.2	23.5	1.5 *	5.9

\* This low rate is due to chance and only the difference between it and the rate for the sulphapyridine group is significant.

suddenly changed from one material to another. Throughout each stage at least two methods of treatment were always in use: the

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M. 53

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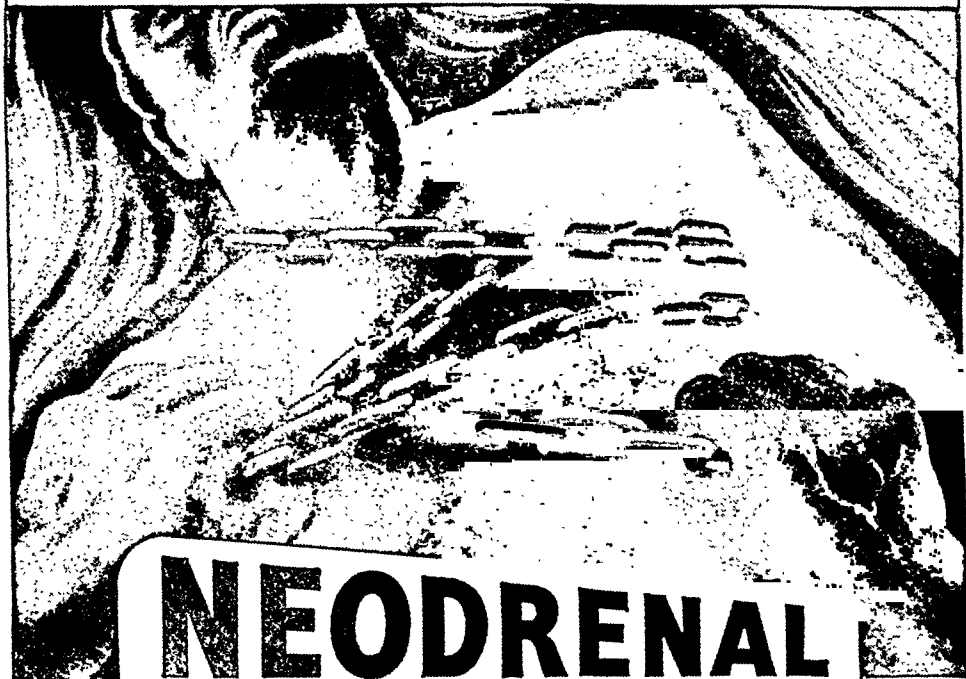
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previously successful one was compared with the newer. Patients received their treatment by alternate allocation to different treatment groups and were not chosen for a particular form of therapy because of their state of illness. A study of the Table permits the immediate conclusion that the change from sulphapyridine to sulphathiazole or sulphadiazine produced immediate benefit. But after this change there was little apparent improvement in the efficiency of the different methods of treatment. Indeed when the cases treated with sulphadiazine or sulphathiazole are compared with those treated with penicillin there is no appreciable difference (Table XII). Such a conclusion is underlined when attention is directed especially to bacteriæmic cases—and here we can be in no doubt of the severity of the disease. It is clear that the results of treatment with sulphonamides compare very satisfactorily with those obtained with penicillin.

TABLE XII

*Direct Comparison of Results with Sulphathiazole and/or  
Sulphadiazine and Penicillin by any Route*

*Sulphanamide.*

Total cases	290.
Total deaths	21. Rate—7.2 per cent.
Cases with bacteriæmia	51. Rate—17.6 per cent.
Deaths in bacteriæmic cases	11. Rate—21.5 per cent.

*Penicillin.*

Total cases	210.
Total deaths	17. Rate—8.1 per cent.
Cases with bacteriæmia	44. Rate—21 per cent.
Deaths in bacteriæmic cases	12. Rate—27.4 per cent.

The standard error of difference for the fatality rates in bacteriæmic cases is  $\pm 7.6$ .

These results induce certain conclusions which may be of basic importance. The first is that further improvements of the chemical side of chemotherapy are unlikely to have much effect upon the mortality from pneumonia. This conclusion is of immediate practical importance for one improvement, recently suggested, may quickly be dismissed. The use of such substances as caronamide in order to obtain higher levels of penicillin in the blood stream will not effect any material improvement upon the outcome in pneumonia. No doubt an enhancement of blood concentration will prove of value when penicillin is used against organisms partially resistant to it: but in pneumococcal pneumonia such enhancement will not improve the results. And, as caronamide is itself a chemical substance with as yet incompletely appreciated side effects, its use in pneumonia seems quite unjustified.

The second conclusion may be drawn from the results obtained with oral penicillin. In many of these patients the blood levels secured



were exceedingly low, yet the effect in a group of patients was comparable with that obtained with other methods of treatment. It would thus seem that in the majority of patients in the adult age-groups effective therapy may be obtained even when less than the supposed optimum amount of penicillin is used. Does this not induce the thought that, in most patients, all that is required to secure effective results is a slight halting of the organism's invasive capacity: once this is secured the host himself can exert his superiority over the bacterium. When the patient fails to recover, it is less the therapy that has failed; and more the host who has failed to implement his share of the bargain. (Such reasoning should, of course, not encourage us to treat a patient lightly, for as I shall emphasise later, we have no effective means of selecting the mild case. To achieve a rapid antibacterial effect should be our immediate desire.)

But a third conclusion may also be suggested. It is generally assumed that, in recovery after chemotherapy, the host achieves the effect by the classical method of the production of specific antibody. It might seem reasonable therefore to suppose that the combination of chemotherapy and sero-therapy should do what improved methods of chemotherapy alone could not do—namely, obtain a further reduction in the fatality rate. Yet in my own hands the fatality rate in bacteraemic type II infections which were given both methods of treatment was 28 per cent.—a figure little different from these shown in Table XI. Clearly the administration of type-specific antibody confers no additional benefit on the severely ill patient. This finding must mean that what prevents recovery in the severe case is not a lack of specific antibody but of some other defensive factor not as yet defined. Indeed one might even go further and suggest that the concept of recovery in bacterial infections as being due mainly or entirely to the formation of specific antibody requires re-examination.

One may conclude by discussing one further aspect of the subject. A question that is frequently asked by students and practitioners is "Which patient should and which should not be treated?" Such a question poses in effect the whole subject of prognosis in acute infections. Now there are few infections of which the mortality—without any form of therapy—is 100 per cent.; that is to say, for most infections there is a natural recovery rate. But, in order to pre-select those patients who will naturally recover, it is essential to be able to point to some recognisable clinical feature always associated with recovery. It is not sufficient merely to show that the mortality rate is less—even very much less—in a group showing one clinical characteristic when compared with another where it is absent. Now in no infection is it possible to point to one such single factor. In pneumonia, particularly, we find that prognosis depends on a compound of characters such as age, extent of lung involvement, condition of the myocardium, type of infecting organism, presence of bacteraemia, and the degree and pattern of leucocytosis. And even when all of these factors are known

the unusual may still occur. The apparently mild case may terminate in meningitis; the seemingly hopeless case may recover. In dealing with acute pneumococcal pneumonia, therefore, every case must be treated. This is particularly true because we know that prior to the introduction of chemotherapy it was not unusual to find that a patient who originally showed a sterile blood culture could, as the disease progressed, eventually develop a bacteriæmia and might, indeed, die. In Christie's series, for example, there were patients whose original blood culture was negative but who went on to develop bacteriæmia and subsequently died. During a recent period, five daily blood cultures were performed on 19 patients who were receiving adequate chemotherapy. The results are shown in Table XIII. Thirteen

TABLE XIII

*Result of Consecutive Daily Blood Cultures in 19 Adult Patients with Pneumonia*

Name	Age	Infecting Organism	Day of Illness.												
			1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.
W.	53	Pneum. ii	...	...	+	—	—	—	—	...	...	...	...	...	...
B.	52	Pneum. i	...	...	o/c.cm.	...	...	+	—	—	—	...	...	...	...
L.	53	Pneum. ii	...	+	+	—	—	o/c.cm.	...	...	...	...	...	...	...
				Not done	2/c.cm.										
C.	37	Pneum. ii	...	...	...	...	...	...	...	+	—	—	+	+	—
										1/c.cm.			Not done	Not done	
McK.	48	Pneum. ii	...	...	...	...	+	—	—	—	—	...	...	...	...
							Uncountable								
McC.	48	Pneum. ii	...	...	+	...	DIED	...	...	...	...	...	...	...	...
					32/c.cm.										

A further 13 cases were negative on admission and on 4 succeeding days.

The note under the culture result refers to the colony-count.

patients were non-bacteriæmic on admission and remained so. One of the six patients with bacteriæmia, however, had his blood initially sterilised, but despite this, bacteriæmia again developed on the fourth and fifth day of therapy. Such occurrences must indicate a need for caution in deciding that chemotherapy may be omitted in a certain type of case.

But if all patients with pneumonia are to some extent in danger, the patient over 40 years of age is particularly at risk. In this age-group the diagnosis of an acute bacterial pneumonia with obvious consolidation should constitute an urgent medical problem and there should be no delay in ensuring that he receives adequate chemotherapy.

### SUMMARY AND CONCLUSIONS

Certain factors in the host-parasite relationship in pneumonia have been considered. Such evidence as we have shows that the causative pneumococci have lost little of their power of invasiveness in recent

years, so that it may reasonably be assumed that chemotherapy must take a large share of the credit for the great lessening in mortality in the middle age periods. Attention is drawn to the continuing high mortality in infancy, and it is argued that the Glasgow experience suggests that pneumonia in the first year of life is not so much a primary infection as an indication of an impoverished host resistance. A survey of the results obtained with sulphonamide and penicillin does not support a view that the latter has any marked superiority over the former. It is felt that the results of therapy are unlikely to be improved further by any enhancement of the efficacy of the therapeutic agents but must depend more upon a study of non-specific factors likely to improve the capacity of the host to withstand a heavy bacterial invasion.

It is a pleasure to acknowledge the help of my junior colleagues, Drs Ferguson, Landsman and Ross. The figures taken from Christie's work will be found in *Lancet* (1933) 2, 804.

# THE HÆMOLYSIS OF ERYTHROCYTES IN SOLUTIONS OF THE ALKALI HALIDES

By EDWARD B. HENDRY, B.Sc., Ph.D., M.B., Ch.B.

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IN a previous paper in this series (Hendry, 1948), the writer has discussed the variables which affect the determination of the standard "hæmolysis curve" in solutions of sodium chloride of varying concentration. It is useful to regard the hæmolysis curve in sodium chloride solution as an arbitrary standard, since both sodium and chloride ions occur in high concentration in blood and are unlikely to have any specific hæmolytic or anti-hæmolytic effects. This assumption may be investigated by replacing each of the ions by a chemically similar ion and observing any alteration in the hæmolysis curve. Only the monovalent ions can be studied in this way; divalent and trivalent ions have special dehydrating effects, and osmotic exchange is further upset by the fact that a divalent ion entering an erythrocyte must expel two chloride or bicarbonate ions in order to preserve electrical neutrality.

## HÆMOLYSIS IN SOLUTIONS OF THE ALKALI HALIDES

The alkali halides are particularly well suited for such experiments. All the ions are monovalent, and, with the exception of the fluorides, all the salts are derived from strong acids and bases and are therefore chemically neutral in solution. Hydrofluoric acid is a weak acid ( $K = 6.9 \times 10^{-4}$  at  $25^\circ \text{C.}$ ) compared with the other halogen acids; solutions of the alkali fluorides therefore tend to have a very slightly alkaline reaction due to salt hydrolysis.

The purest available specimens of the various salts were used. If the purity were in any doubt, the salt was recrystallised from water. Standard solutions of the alkali halides cannot always be made up directly from the dried salt. Lithium chloride has the well-deserved reputation of being the most deliquescent salt known in chemistry, and sodium iodide suffers from the same disadvantage. Solutions of approximately four times the required concentration of these two salts were made up and standardised gravimetrically with silver nitrate; working solutions were prepared by accurate dilution of the stock solutions and the working solutions were further checked before use by means of standard silver nitrate (chromate indicator). Solutions of the other salts were made up directly from specimens which had previously been dried to constant weight, thus ensuring, amongst other things, the removal of water of crystallisation from the dihydrate of

sodium bromide. In this paper, all concentrations and weights are expressed in terms of the *anhydrous* salts.

In calculating the osmotic pressures of solutions of the alkali halides, the necessary data has been obtained from the *International*

TABLE I

*Hemolysis Curves of Normal, Oxygenated Human Blood (Oxalated) at 18-19° C. Dilution = 1 in 20. Time of Hemolysis = 1 hour. Results Expressed in Terms of Concentration (gm. per 100 c.c.)*

Salt.	Molecular Weight.	Number of Curves.	Percentage Hemolysis.				
			10.	30.	50.	70.	90.
LiCl	42.4	5	0.276	0.262	0.253	0.245	0.231
NaF	42.0	5	0.332	0.313	0.299	0.286	0.246
NaCl	58.5	20	0.395	0.376	0.366	0.354	0.332
NaBr	102.9	5	0.698	0.652	0.633	0.614	0.577
NaI	149.9	5	0.984	0.923	0.891	0.859	0.796
KCl	74.6	8	0.540	0.518	0.500	0.485	0.449
KBr	119.0	5	0.825	0.787	0.766	0.745	0.699
KI	166.0	5	1.121	1.066	1.031	0.997	0.917
RbCl	120.9	5	0.861	0.818	0.799	0.775	0.721
CsCl	168.3	5	1.159	1.085	1.046	1.011	0.944

TABLE II

*Hemolysis Curves as Described Above. Results Expressed in Terms of Osmotic pressures (Atmospheres at 18° C.)*

Salt.	Factor (see Text).	Percentage Hemolysis.				
		10.	30.	50.	70.	90.
LiCl	10.57	2.92	2.77	2.67	2.59	2.44
NaF	10.71	3.56	3.35	3.20	3.06	2.63
NaCl	7.69	3.04	2.89	2.81	2.72	2.55
NaBr	4.38	3.06	2.86	2.78	2.69	2.53
NaI	3.05	3.00	2.81	2.72	2.62	2.43
KCl	6.03	3.25	3.12	3.01	2.92	2.70
KBr	3.77	3.11	2.97	2.88	2.81	2.64
KI	2.71	3.04	2.89	2.80	2.70	2.49
RbCl	3.65	3.14	2.98	2.92	2.83	2.63
CsCl	2.65	3.07	2.88	2.77	2.68	2.50

*Critical Tables* (1929). Both freezing-point depression and conductivity measurements have been examined. In general, there is good agreement between the two methods—sodium fluoride being the only notable exception, and for this salt, freezing-point depression measure-

ments give values 7 per cent. higher than do conductivity measurements. The mean values have been used for this salt. The data for sodium iodide are somewhat scanty over the required range, but for the other salts, the data are sufficient and the agreement excellent.

Throughout the present series of experiments, oxalated blood from normal adult humans (blood donors) has been used. Hæmolysis curves have been determined using a solution of 1 : 20 of fully oxygenated blood in a series of dilutions of the hæmolysing salt solution. Hæmolysis was allowed to proceed for one hour at 18-19° C. except in the case of sodium chloride where the duration of hæmolysis was two hours, and the temperature 19-21° C., the extra time of hæmolysis almost exactly counterbalancing the increased temperature. The percentage hæmolysis in each tube was determined by the method already described (Hendry, 1947). For any given salt there is very good agreement among a series of hæmolysis curves of normal bloods in solutions of that salt.

Tables I and II give the results of a series of such experiments. In Table I, the results are expressed in terms of concentration; in Table II these concentrations have been converted to terms of osmotic pressures. Over the small range of concentrations concerned, the osmotic pressure is proportional to the concentration for all practical purposes, and the factors used to convert the latter to the former are given in the second column of Table II, *i.e.* for sodium bromide, the osmotic pressure (in atmospheres at 18° C.) =  $4.38 \times$  the concentration (in gm. per 100 c.c.).

Fig. 1 shows the hæmolysis curves in solutions of the alkali chlorides; Fig. 2, the hæmolysis curves in solutions of the sodium halides.

The full significance of these curves is not clear; their immediate practical importance lies in the fact that they enable one to interchange cations and anions with predictable results. The curve in sodium fluoride is outstandingly different from all the other curves and this difference must be due to an effect of the fluoride ion since the curves for the other three sodium halides lie remarkably close together. The *pH* of the hæmolysing system is not an operative factor. Numerous determinations of the *pH* were made on random samples of the mixture of blood and solutions of all ten salts studied, and it invariably lay within the limits 7.9-8.2. When blood is added to sodium fluoride solution (dilution = 1 : 20) the blood buffers are sufficient to overcome the very slight alkalinity of this salt and maintain the *pH* within the above-mentioned limits.

According to Wilbrandt (1940) sodium fluoride increases the osmotic resistance of erythrocytes (*i.e.* decreases the tendency to hæmolysis). Unfortunately, his paper is not accessible nor can reference be found to it in the various abstracts. Höber (1945, p. 251), however, refers to Wilbrandt as having reported an "enormous increase of osmotic resistance" after addition of sodium fluoride to a

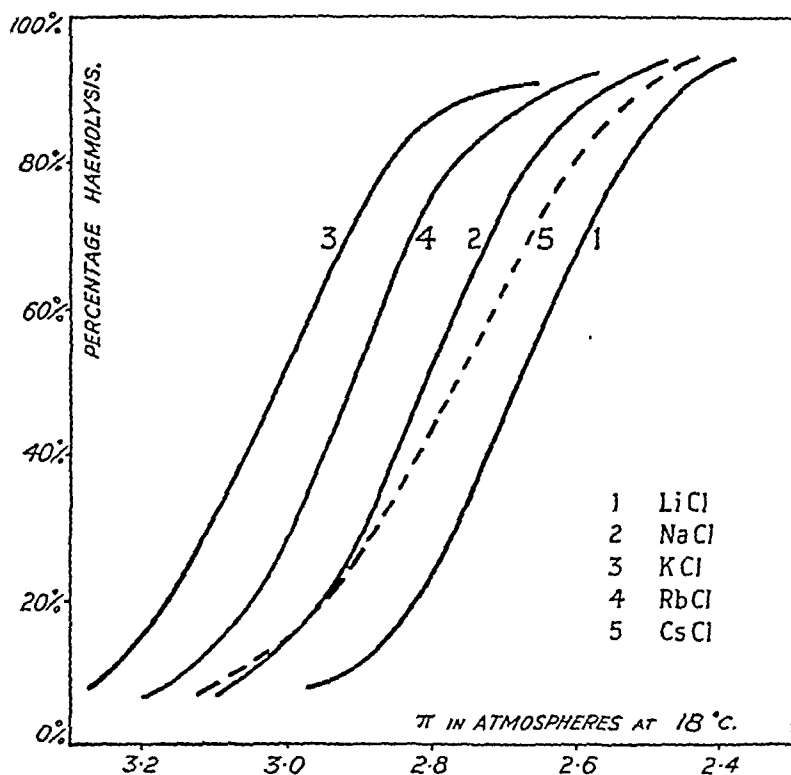


FIG. 1.

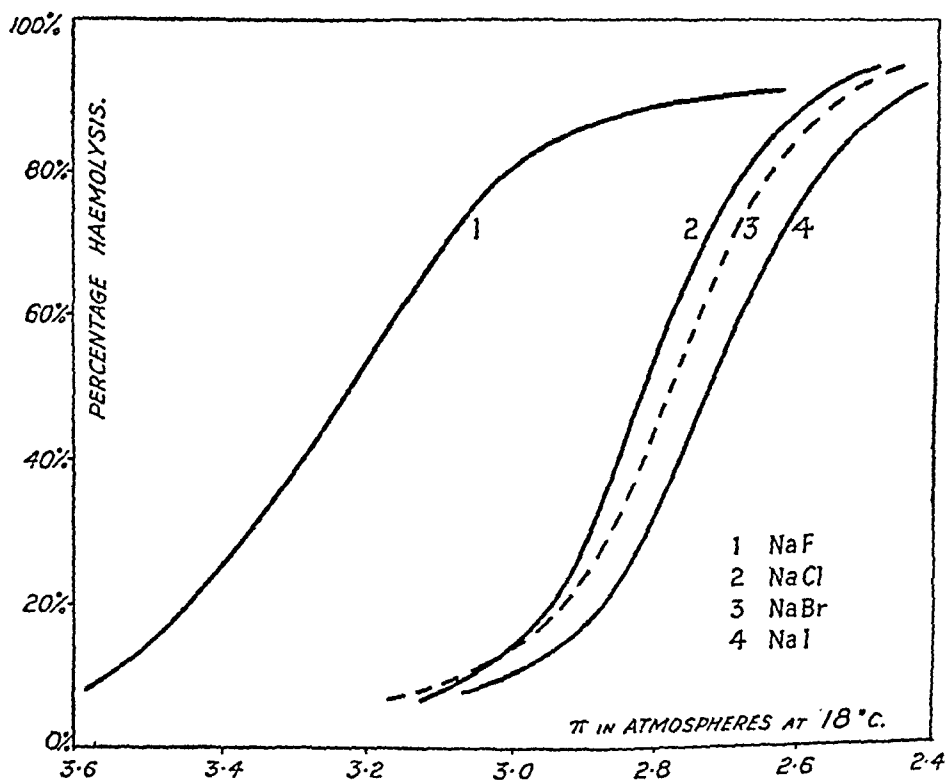


FIG. 2.

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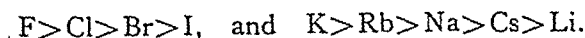
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suspension of human erythrocytes in saline. Iodoacetate was found to have a similar action. These effects are ascribed to the interference of these compounds with the normal processes of glycolysis, and it is suggested that the breakdown of glucose plays an important part in reducing permeability. In the experiments described above, there can be little doubt that glycolysis is completely inhibited by the concentrations of fluoride used, and yet, hæmolysis occurs much more readily in sodium fluoride than in any of the other sodium halides, *i.e.* the osmotic resistance in fluoride is much lower than in chloride, bromide or iodide. The results are unequivocal and the difference between fluoride and other halides is most pronounced. The effect of fluoride, as indicated by the position of its hæmolysis curve, is more in keeping with the expectation that it would be more hæmolytic than the other halides on account of its smaller ionic volume and consequently (since it is an anion) its greater ease of penetration into the cell.

The order of hæmolytic activity of the anion series is  $F > Cl > Br > I$ ; and of the cation series  $K > Rb > Na > Cs > Li$ . Since the erythrocyte membrane is freely permeable to anions, the order of hæmolytic activity of the anions may be explained in terms of ionic volume. The order in the series of cations cannot be explained either in terms of ionic volume or ionic mobility, but the same order of activity is not unknown in biological experiments. The same series has been found to have an increasingly stimulating effect on isolated frog muscle; approximately the same order (with sodium and cæsium transposed) determines the dispersion of lyophilic colloids, and the potential difference along a nerve fibre when one end is dipped in potassium chloride solution and the other into a solution of an alkali chloride (see Höber, pp. 290, 293, 314).

### SUMMARY

1. A study has been made of the hæmolysis curves of normal human erythrocytes in solutions of the alkali halides. The ions, in order of increasing hæmolytic activity, follow the series



2. The observation that fluoride increases the osmotic resistance of erythrocytes, has not been confirmed.

The author is grateful to the Earl of Moray Fund of the University of Edinburgh for a grant which helped to defray the expenses of this work.

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## DISEASE OF THE UPPER AIR PASSAGES IN RELATION TO PULMONARY TUBERCULOSIS

By D. BROWN KELLY, M.D.

A FEW months ago at a meeting of the Southern Medical Society, Glasgow, an excellent paper on pulmonary tuberculosis was given by my friend Dr Frew. In the discussion which followed, I humbly inquired as to the advisability of treating non-tuberculous disease of the respiratory tract (such as sinusitis) in patients with phthisis. The replies to my question were varied, but the majority seemed to indicate that on no account were such patients to be permitted to fall into the hands of the E.N.T. surgeon.

I feel all the more honoured, therefore, at being allowed to address you to-day, to have the opportunity of laying the facts before you as viewed by the rhinologist, and of inviting discussion, criticism and advice. If I can do this, then my object in preparing this short paper has been achieved. Considering that every cubic centimetre of inspired air passing to the diseased lungs of your patients has to pass through the upper air passages, surely the health of these structures is of paramount importance.

In this age of specialisation, one is sometimes inclined to forget that the respiratory tract is a continuous system. From the literature and from the general attitude towards infection, it might almost be concluded that the upper and lower respiratory passages were separate systems.

This fact is remarkably demonstrated in the history of medicine. For instance, bronchiectasis was recognised by Laennec as far back as 1819, and the existence of nasal sinusitis was known certainly in 1707, through the work of William Cowper, and yet it was not until 1914 that the connection between the two was demonstrated by St Clair Thomson. The fact that the conditions are closely associated is now universally recognised. Indeed McLaurin in 1932 maintained that almost 100 per cent. of all cases of tracheo-bronchitis, bronchiectasis, and peri-bronchial infection are dependent on chronic sinus disease.

In the course of routine ear, nose and throat examination of several hundred patients in this Sanatorium, I have been confronted with the problem of upper respiratory tract disease, and have wondered what effect a blocked nose or a chronic post-nasal purulent discharge can have on patients with pulmonary tuberculosis. The problem is mainly one of treatment. Is surgical interference warranted in dealing with such cases? References on this question in the literature are hard to find, and the problem is one I would like to put before you now.

Read to the Tuberculosis Society of Scotland 18th June 1948.

The morbid conditions coming into review in this respect may be roughly classified into three groups. First, those causing nasal obstruction. Secondly, nasal and naso-pharyngeal sepsis—often accompanied by obstruction, and lastly septic conditions of the mouth and pharynx.

For many years now, physicians have realised that a healthy, unobstructed nose is of prime importance to the development of a sound chest and a healthy individual. Few children with buccal breathing can nowadays escape adenoidectomy, and almost the first thing the general practitioner does when confronted with a child who is slow in developing is to refer him for removal of tonsils and adenoids.

It is necessary to emphasise that the nose is far more than an olfactory organ. It warms, moistens and humidifies the inspired air. It acts as a filter against dust and bacteria which, if not arrested at the nares, are caught in the mucous blanket covering the whole lining of the nose and swept by the cilia into the pharynx. If the nose be obstructed, cold, unmoistened, unfiltered air passes direct to the bronchi and lungs.

The most common forms of nasal obstruction encountered here are turbinal hypertrophy, polypi and deviations of the septum. The latter condition may be misleading. The patient being able to breathe through the wide side of his nose, does not complain of obstruction. If, however, the deviation be severe, this wide side will be too patent, and the inspired air will pass through it too quickly to allow proper warming and moistening to take place. Chronic pharyngitis and laryngitis frequently accompany this state of affairs.

As regards treatment, cauterisation of turbinates and removal of nasal polypi present no great difficulty, being minor procedures under local anæsthesia and causing little upset to the patient. Resection of the septum might be indicated in severe cases attended by much irritation contributing to the cough. The operation, unlike tonsillectomy, leaves no open wound, and is also carried out under a local anæsthetic.

The patients on whom these procedures are carried out, should of course be carefully selected, and where there is any likelihood of the chest condition being aggravated by even minor surgery, then operation is contra-indicated.

I come now to what is probably the most important group of the diseases under consideration, namely, chronic nasal sinusitis. This infection is associated with the production of pus or muco-pus which passes down the back of the pharynx to be swallowed, or what is worse, to pass the barrier of the larynx during sleep and penetrate to the trachea and bronchi. This post-nasal discharge can give rise to innumerable complications, as it is often laden with virulent bacteria. Chronic granular pharyngitis and chronic laryngitis are frequent sequelæ. Gastric disorders follow the ingestion of the pus. General malaise and mental depression are common symptoms, but it is the effect on the chest which is of primary importance.

There are four possible routes by which infection may travel from the nose to the bronchi—by aspiration, direct extension by continuity of mucous membrane, by lymphatics and by the blood stream. In 1929, Quinn and Meyer dropped iodised oil into the nostrils of 11 sleeping patients. In 5 the oil penetrated to the lungs. If a foreign substance such as lipiodol can pass the larynx without causing a cough reflex, a post-nasal discharge to which the larynx has become accustomed can surely do so.

The effect on a patient with pulmonary tuberculosis is serious. In addition to his combat with the tubercle bacillus, he must contend with innumerable pyogenic organisms. He already has a cough due to his pulmonary complaint. This is aggravated by irritation from a chronic pharyngitis and laryngitis. The larynx is rendered more liable to infection by the tubercle bacillus, being kept in a state of chronic irritation with resultant coughing, and being bathed in mucopus.

Sinus disease not only has an adverse effect on the tuberculous patient, it may give rise to a chest condition very similar to phthisis in its symptoms and physical signs. Thus D'Eloia recorded in 1940: "Sinusitis and tuberculosis both produce the same symptoms especially in children—pallor, restlessness, irritable disposition, unproductive night and morning cough, poor appetite and frequent colds." He also stressed the frequency of asthma in hyperplastic sinus disease.

Brock and Bell in the *American Review of Tuberculosis* for 1938, admitted that many cases sent into a Sanatorium for differential diagnosis are shown to have a chronic tracheo-bronchitis caused by repeated infection from the upper respiratory tract. Other patients, admitted to hospital with a diagnosis of pulmonary tuberculosis, particularly those with upper lobe lesions and negative sputum, have proved to be cases of bronchiectasis.

In one series of 253 tuberculous patients, 101, or 40 per cent. had disease of the nasal sinuses. The authors admit that this high incidence may be due to the climatic conditions of the locality from which the patients were drawn (Louisville).

The incidence in this country is not nearly so high. Out of the last 250 patients seen by me in this Sanatorium, only 10 have shown definite clinical signs of sinusitis. Antral disease is treated by proof-puncture and lavage, care being taken to see that there is no dental disease responsible for the infection. Drainage of frontal and ethmoidal cells is improved by conservative measures such as positional ephedrine treatment. Fortunately there has been no occasion for major sinus surgery. Sanatorium life plays a large part in the healing of infected sinuses. The fresh air, especially the absence of central heating with its deleterious effect on the nasal mucosa, the regular diet and ordered mode of life are all beneficial in this respect.

There are some interesting points in connection with the X-ray examination of patients with chest conditions due to infected sinuses. Wesson and others have compared the radiological appearances in

tuberculosis and broncho-sinus disease. They recognise a definite chest picture which seems to be associated with chronic nasal infection. This shows an increased density at the hilum and of the bronchial and perivascular markings combined with shadows at the base of the lung. These basal shadows are continuous with those of the hilum, and extend downwards along the border of the mediastinum to the diaphragm. The term pneumonitis has been applied to the condition. Such a chest picture enables the trained radiologist to foretell the state of the patient's sinuses with some degree of accuracy.

Finally I should like to mention briefly conditions of the mouth and pharynx. The two common complaints met with here are dental sepsis and tonsillitis. A healthy mouth is essential for the patient's well being. Not only will dental caries and pyorrhœa exert a toxic effect, but inability to masticate food will predispose to gastric disorders. It is important, therefore, to see the patient can masticate his food and that his teeth are in good order or that he has well-fitting dentures. In this Sanatorium full dental treatment is carried out, and I understand that no ill effects have resulted from extractions, which are done under local anæsthesia, only one or two teeth being removed at a sitting.

Tonsillectomy in a patient with active phthisis is, in my opinion, hardly ever justified. It might be permissible in tuberculous ulceration of the tonsil, where there is a reasonable hope of recovery as regards the chest condition.

Repeated attacks of tonsillitis—the chief deciding factor in tonsillectomy, are rare under sanatorium conditions where the risk of infection from other individuals is at a minimum. Further, the large raw areas left after operation may become invaded by the tubercle bacillus in the sputum giving rise to a virulent tuberculous pharyngitis and miliary spread. Dr Baxter tells me he has known of two such cases which died a few weeks after operation.

Pinkerton, in the *Trans. Amer. Laryng. Soc.* for 1935 expresses the opposite view, which may be of interest to mention as a contrast.

In a paper based on 102 tonsillectomies under local anæsthesia, he maintains that if the tonsils are greatly enlarged, or the seat of an ulcerative process, the patient's condition should be carefully reviewed. The extent of the tuberculous infection, the general trend towards healing or progression, and the activity of the lesion are taken into account. If, after careful weighing of these factors, it is considered that tonsillectomy can be done without affecting the condition unfavourably, and with the possibility of removing an obstruction in the way of recovery, operation should be carried out. If there is actual tuberculosis of the tonsil, the eradication of this nidus of disease hastens recovery, and is not dangerous if the cases are carefully selected and the operation skilfully performed.

Positive tonsil specimens were obtained in 29 cases, with a preponderance of the deep hyperplastic type. Caseo-ulcerative disease

was present in two, and miliary in one instance. There were two deaths, one three years after operation, following a thoracoplasty, and the other two months after tonsillectomy due to heart failure.

The symptoms of chronic focal sepsis arising from infected tonsils are, like sinusitis, very similar to those of early tuberculosis. One must avoid indiscriminate tonsillectomy in young adults with indefinite symptoms suggestive of a septic focus. Unless a careful general examination be carried out, the real cause of the patient's ill-health, namely early phthisis, is missed. Philips records 34 cases in which pulmonary tuberculosis became manifest within two years of tonsillectomy. The patients in fact probably had the disease before operation. Possibly the operation did little harm—indeed the enforced rest in bed may have benefited the patient. The trouble was that something had been done, the surgeon and patient put off their guard, and the patient went on to a serious breakdown because the diagnosis had been missed.

So, gentlemen, once again I welcome discussion on this point. A patient with pulmonary tuberculosis is not progressing as well as he should. He has an obstructive or septic condition in his upper air passages. Might not treatment of this lesion just tip the scales in his favour by removing the constant drip of pus into his larynx, or by ensuring that the air reaching his diseased lungs is properly conditioned.

## TUBERCULOUS PERICARDITIS

By THOMAS SEMPLE, M.D., B.Sc., M.R.C.P.(Edin. & Lond.), F.R.F.P.S.

*From the Victoria Infirmary, Glasgow, and the Thoracic Unit,  
Hairmyres Hospital*

THE objects of this short paper are to stress firstly that tuberculous pericarditis is probably less unusual than commonly believed; that in the acute stage it may produce a relatively mild illness which can easily pass unrecognised as such; and that, as recently confirmed by various writers,<sup>1, 2, 3</sup> Pick's syndrome of chronic pericardial compression may be due to subacute tuberculosis but is more commonly related to old healed tuberculosis of the pericardium.

One does not consider tuberculosis the only cause of Pick's syndrome, for it has been known to occur following septic pericarditis, and in the literature one finds reports of the syndrome caused by invasion of the pericardium by malignant processes,<sup>4</sup> Hodgkin's disease,<sup>5</sup> tularæmia,<sup>6</sup> actinomycosis,<sup>7</sup> and foreign body.<sup>8</sup> It has long been accepted that rheumatic pericarditis does not produce the syndrome. In rheumatic fever,<sup>9</sup> and pyopericardium,<sup>10, 11</sup> diffuse symphysis does occur between the pericardial layers yet such adhesions rarely produce symptoms and signs during life. Apparently after such infections, the pericardium retains its elasticity while with tuberculous involvement, the membrane becomes rigid as well as thickened. When this occurs, tamponade may be produced by (1) effusion developing within the rigid serous membrane; (2) thick granulation and caseous material; (3) adhesions; (4) contraction of chronic granulation tissue and inflamed pericardium. At operation, we have seen all these factors in play at one time.

It is interesting to learn what was known of pericardial disease by the older clinicians: Galen around A.D. 160<sup>12</sup> described pericardial effusion in a monkey and scirrhus thickening in a cock and surmised that the same conditions might occur in man. He was probably the first to operate on the pericardium in man when he removed part of the diseased sternum and a piece of pericardium in a case of post-traumatic anterior mediastinitis. In 1669, Richard Lower<sup>13</sup> gave the first account of pericardial disease in man. He described tamponade due to effusion and the effects of adhesion and constriction. Just over a hundred years ago, in 1842, Chevers<sup>14</sup> described in *Guy's Hospital Reports*, the cardiac failure of the small heart in the absence of valvular disease. He published clinical and autopsy findings in a girl of 18 years, who died with generalised tuberculosis and constrictive pericarditis. He recognised that "the failure was due to contraction

Read before the Tuberculosis Society of Scotland, May 1948



of adhesive matter, compressing muscular tissue and embarrassing systole and diastole, more particularly the latter."

More recent writings indicate that pericardial involvement in tuberculosis is closely related to mediastinal gland disease. In this connection, it is interesting to note that tuberculous pericarditis is relatively common in Africans. Heimann and Binder,<sup>15</sup> in 1940, described 31 cases in Bantu natives, with 28 autopsies, and in all of the latter, tuberculous mediastinal root glands were found. High mortality was related to the bad prognosis of the primary tuberculous complex in primitive peoples. Root glands on the right side were involved more frequently, and in this connection one should mention Shore's description<sup>16</sup> of a "caval gland of the heart," lying above the right lung root, receiving lymph drainage from both the lung and the heart. Retrograde lymphatic spread from this gland is postulated and in the Bantu series, tuberculous involvement of interpolated intrapericardial lymph glands was found. In ten of the post-mortems, there was tuberculous affection of the myocardium, most commonly in the wall of the right auricle.

The following patients would seem to illustrate various stages in the development and course of the disease :

*Firstly, the stage of Fibrinous Pericarditis :*

CASE 1.—R. T., aged 14, was admitted to hospital in November 1947. X-ray showed a typical Ghon focus in the right upper lobe with hilar gland enlargement. B.S.R. was 46 mm. but gradually subsided. He had had acute rheumatism three years before and now had a frank mitral stenosis. The present illness started with pains in the toes and hips in September 1947, but after this he had no symptoms, was afebrile and indeed had no signs of general ill health. A week after admission to hospital, however, he had coarse pericardial friction which lasted three days but at this time he was so well that a diagnosis of rheumatic pancarditis seemed quite untenable. Convalescence was uneventful.

*The next two cases are examples of Pericarditis with Effusion :*

CASE 2.—A. K., aged 11, developed a deep barking cough at the beginning of December 1947, and his doctor discovered he had coarse pericardial friction although he seemed otherwise perfectly well. He came under observation in hospital a fortnight after this. Apart from a deep bovine cough and occasional profuse sweatings for a few weeks, he had no symptoms. He was bright, intelligent and always said that he felt fine. On admission he had clinical signs of pericardial effusion and coarse friction. X-ray confirmed the presence of effusion and also showed a Ghon focus in left upper lobe with corresponding root gland enlargement. Low grade fever and pericardial friction lasted for a fortnight after admission and effusion then rapidly cleared. Convalescence was satisfactory and serial X-rays showed hardening of the primary complex.

CASE 3.—I. G., a Sales Driver, aged 27, was admitted to hospital in April 1947, with a story of fourteen days pain in the precordium. This vanished soon after admission. He was well nourished and never looked nor felt ill.

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tryptophane	..	0.3%	..	1.0%
phenylalanine	..	0.9%	..	3.0%
cystine	..	0.3%	..	1.0%
methionine	..	0.5%	..	1.6%
threonine	..	1.2%	..	4.0%
leucine..	..	2.1%	..	7.0%
isoleucine	..	1.3%	..	4.3%
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# Bronchitis

## Winter Cough and Sequelæ

There is a vast amount of evidence of the most positive character proving the efficacy of Angier's in sub-acute and chronic bronchitis. It not only relieves the cough, facilitates expectoration, and allays inflammation, but it likewise improves nutrition and effectually overcomes the constitutional debility so frequently associated with these cases. Bronchial patients are nearly always pleased with Angier's and often comment upon its soothing, "comforting" effects. The unique soothing properties of Angier's, its favourable influence upon assimilation and nutrition, and its general tonic effects, make it eminently useful both during and after influenza. It has a well-established reputation for efficiency in relieving the troublesome laryngeal or tracheal cough, correcting the gastro-internal symptoms and combating the nervous depression and debility.

## Angier's Emulsion

Temperature was never over 99° F. He was found to have a pericardial effusion but he had no dyspnoea, cyanosis nor oedema.

X-ray showed pericardial effusion, congested hilar region and a right pleural effusion. A coarse pericardial friction rub remained for ten days after admission. Aspiration of pleural effusion produced a lymphocytic exudate. After three weeks there was considerable reduction in pericardial fluid, B.S.R. had fallen from 40 mm. to 6 mm., and he was allowed up. He was allowed home after four weeks and X-ray showed a normal heart shadow apart from some apparent enlargement of left auricle, suggesting mitral stenosis.

These last two patients illustrate the misleading mild course of events when a pericardial effusion develops in relation to tuberculous infection. It has many points in common with the more easily recognised tuberculous pleurisy with effusion. For instance, it is recognised<sup>17</sup> that both have a much more grave prognosis when tubercle bacilli can be isolated from the fluid.

CASE 4.—A. B., a male aged 47, had Pick's syndrome related to a pericardial effusion in association with a tuberculous empyema. The fluid contained R.B.C. and pus cells and yielded the tubercle bacillus. He died four months after admission to hospital but even here temperature was never over 99.5° F. (Fig. 1).

The remaining five patients in the series have had the operation of pericardial resection for varying degrees of Pick's syndrome. The signs of this condition are in the main due to a low intake of blood to the heart owing to limitation of diastolic filling by the constricting membrane. The immediate effect is a damming back of blood in the veins with a rise of venous pressure. Oedema is an inconstant feature and its presence probably depends on additional factors, such as plasma protein levels.<sup>18</sup> Liver enlargement and ascites are constant and this may be related to the absence of valves in the hepatic veins, with consequent increased pressure and stasis in the intralobular veins and sinusoids. Pulsus paradoxus is characterised by marked diminution or complete disappearance of the pulse wave in inspiration and the dynamic theory of Hitzig<sup>19</sup> is worthy of more general recognition:

In the normal individual, there is a relative ischaemia of the pulmonary vascular bed during inspiration. Owing to the diminished right ventricular output in pericardial tamponade, this relative ischaemia is exaggerated and so there is very little blood returned by the pulmonary veins. Left-sided diastolic filling and consequently systolic output is therefore greatly diminished during inspiration.

Low blood pressure and low cardiac output are corollaries to poor diastolic filling. The fluid in pleural and abdominal cavities may be transudate, related to venous congestion, or exudate due to tuberculous serositis.

CASE 5.—J. McD., male aged 12, had been in another hospital for four months with pericarditis about a year before admission with classical signs

of Pick's syndrome. An older sister had pulmonary tuberculosis. X-ray (Fig. 2) showed fluid in both pleural cavities with perihilar thickening and a broad upper mediastinal shadow, especially to the right.

On admission he was very œdematous and venous pressure was raised to 25 cms. He had a very good response to mersalyl, œdema and ascites diminishing but liver remaining down to umbilicus. Pericardectomy produced almost immediate disappearance of œdema, ascites and pulsus paradoxus. Histological examination of pericardium (Fig. 3) showed chronic inflammatory cell infiltration with no evidence of tuberculous involvement. He was up after a fortnight and convalescence was uneventful till six weeks later when he developed a synovial tuberculosis of the left elbow joint.

CASE 6.—H. R., a schoolmaster, aged 47, first developed signs of cardiac failure in January 1946, but these cleared after eight weeks' rest in bed. They recurred five months later when pleural and peritoneal effusions were found to be exudative in character but negative for tubercle bacilli. From then until November he was not confined to bed and felt quite well but he required abdominal paracentesis at fortnightly intervals.

On examination in November 1946, he had a Pick's syndrome associated with moderate pericardial effusion. Samples of fluid from pericardium, pleura and abdomen were negative for tubercle bacilli. Mantoux test was also negative. Tomograph at 8 cms. (Fig. 4) showed a rounded focus in the right lung field, very like a healed Ghon lesion. The effect of pericardectomy here was striking and on discharge home four weeks later, the only abnormal finding was residual liver enlargement. Histological examination of pericardium showed thick fibrous tissue with plasma cells and a few aggregations of lymphocytes. X-ray seven months later showed a normal heart shadow. He reported in April 1948, when he had been doing a full day's work since May 1947, with no symptoms.

CASE 7.—J. G. R., a chef aged 23, had tuberculous peritonitis found at laparotomy when six years old. Following this he always had slight dyspnœa and œdema of ankles which restricted him hardly at all even at active games. In 1942 he was serving in the Navy and after a rough time in a convoy, he was admitted to hospital in Malta with a mild pyrexial illness. He was X-rayed, pericarditis was diagnosed and he was invalided from the Service. His symptoms then and later were no more severe than they had been for years. While in Switzerland in 1946, a Cardiologist told him he had constrictive pericarditis and advised operation. When seen in July 1947, his general condition was excellent. There was clinical and radiological evidence of heart enlargement and he had pulsus paradoxus and slight œdema of ankles. There was no liver enlargement nor increase of venous pressure. A pint of clear lymphocytic fluid was aspirated from the pericardium and was negative for tubercle bacilli. Pericardectomy was performed on pressure from the patient, owing to the possibility of development of classical constrictive pericarditis. Histological examination of pericardium showed only chronic inflammatory, non-specific, granulation tissue. Convalescence was uneventful. The œdema of ankles which may have been in part related to an old-standing thrombo-phlebitis, did not subside.

In these last three cases, one might be excused for objecting that a tuberculous aetiology has been no more than presumptive. The next



FIG. 1.—Tuberculous pyopericardium and empyema. Air replacement outlines greatly thickened pericardium.

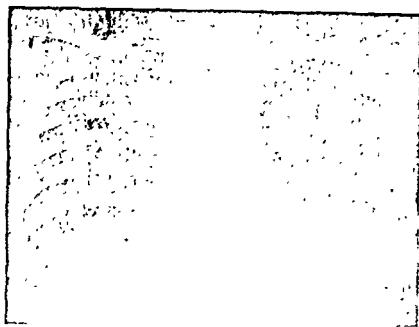


FIG. 2.—Example of Pick's syndrome before treatment. Note congestive changes and pleural effusions.



FIG. 3.—Section of pericardium from case of probable tuberculous constrictive disease. Note non-specific chronic inflammatory changes.  $\times 52$ .

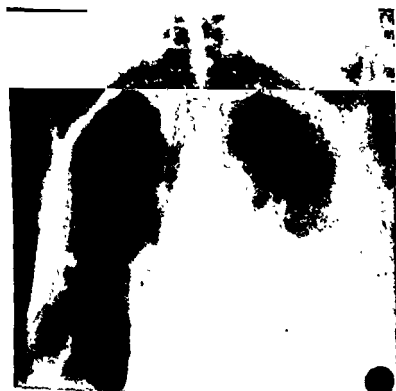


FIG. 4.—Pick's syndrome. Tomograph at 8 cms., showing probable healed Ghon focus in right lung. Note also pleural effusions.

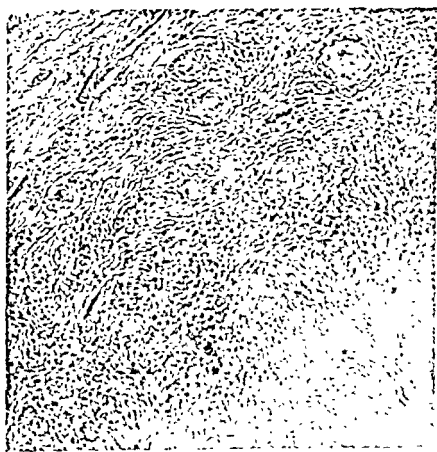


FIG. 5.—Section of pericardium from case of tuberculous constrictive disease. Note typical follicles and caseation.  $\times 65$ .





FIG. 6. — Tuberculous constrictive pericarditis before operation (case 8).

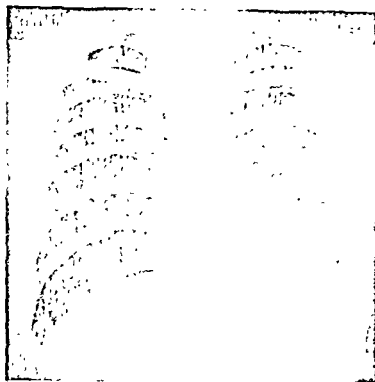


FIG. 7. — Case 8 nine months after operation. Paralysis of the left hemidiaphragm is a common complication, due to implication of the phrenic nerve during pericardectomy.

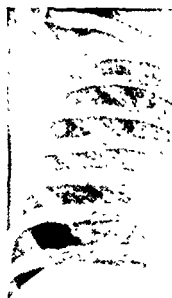


FIG. 8. — Case 9. Tuberculous constrictive pericarditis. Heart shadow is enlarged and there is a left-sided pleural effusion. The right hilar shadow is caused by an interlobar fluid collection and possibly glands in addition.



FIG. 9. — Case 9. Section after pericardectomy showing fibro-caseous tuberculous disease.  $\times 52$ .



FIG. 10. — Lateral view of chest showing calcified pericardium.





two patients illustrate Pick's syndrome caused by histologically proved tuberculous pericarditis.

CASE 8.—R. McL., a private aged 20, had the operation of pericardectomy in December 1947. Histological sections (Fig. 5) showed typical tuberculous follicle arrangement. His illness had started sixteen months before while serving in Middle East. He had a long-standing pyrexia with pleural effusions and was invalided to U.K. after six months. Samples of sputum and of fluid from pericardium and pleura were negative for tubercle bacilli. By May 1947, there was no remaining fluid in pericardium but ascites had developed and this fluid yielded the tubercle bacillus on guinea-pig inoculation. Venous pressure was 33 cms. but œdema was never present. Fig. 6 shows the radiological appearances of the chest before operation, and Fig. 7 is taken nine months later.

CASE 9.—G. M., a boy aged 13, developed digestive trouble, dull pain in the right chest and vague signs of general ill-health in May 1946. By September he was dyspnoëic on exertion and was found to have a large cardiac shadow on X-ray. By February 1947, he had signs of constrictive pericarditis with moderate heart enlargement (Fig. 8) but no œdema. Aspiration attempts produced no pericardial fluid.

During seventeen weeks in hospital, his condition showed little change. While it was thought that the condition was probably tuberculous, samples of fluid from abdomen and left chest were negative on guinea-pig inoculation, Mantoux test was negative and temperature and E.S.R. remained normal throughout. The effect of mersalyl had been tried with little or no beneficial result.

At operation, the pericardium and left diaphragmatic pleura were found to be studded with tubercles. The pericardium was grossly thickened with adhesion and loculated fluid. Pieces of pericardial tissue were sent to two laboratories; one reported a chronic infective, non-specific granulomatous process and the other, fibro-caseous tuberculous disease (Fig. 9). All abnormal physical signs with the exception of hepatic enlargement gradually disappeared after operation and, rightly or wrongly, he was allowed up a month later. The operation took place in June 1947; in October, Mantoux test was still negative (second strength P.P.D.). In December, he developed a right pleural effusion almost certainly tuberculous and related to over-indulgence in exercise. After this he was kept to a strict sanatorial regime and gradually improved. By March 1948, Mantoux test was positive (first strength P.P.D.). He was discharged from hospital, free of complaints, in May 1948.

CASE 10.—D. C., a domestic servant aged 40 had an operation in 1945 for calcified pericardium with associated Pick's syndrome. There was no history of previous ill-health. A recent skiagraph (Fig. 10) still shows well-marked calcification. There is a moderate degree of residual Picks' disease but she has no complaints and is well pleased with the result.

There is some doubt as to the aetiology of the calcification of the pericardium; the older textbooks claim it to be usually the result of pyopericardium but more recent literature<sup>20</sup> suggests that here also we have a late effect of tuberculous pericarditis.

## CONCLUSION

Holmes Sellors and Ellman, amongst other writers, have pointed out that a tuberculous pericarditis with effusion may not yield the tubercle bacillus on guinea-pig inoculation. Suzman has found the Mantoux test negative in a case of pericardial effusion, proved at autopsy to be tuberculous. Our findings confirm these observations and the belief<sup>17</sup> that where the organism cannot be isolated, prognosis is correspondingly more favourable.

That tuberculous pericarditis is a predominantly male disease, is amply supported.

As constrictive pericarditis appears years after the initial mischief, it rarely falls to the lot of one observer to follow the change, but I submit that these cases illustrate the chief stages of fibrinous, serous, subacute fibrocaseous and chronic fibroid disease. It is in general medical wards and outpatients that we must look for the early cases and there is some evidence that aspiration of the effusion with air replacement has a place in prevention of late sequelæ.<sup>23</sup>

It should be remembered that Pick's syndrome bears more than a superficial resemblance to mitral stenosis with cardiac failure. On radiological examination, an exaggerated auricular impression on the œsophagus may sometimes be encountered,<sup>24</sup> due not to enlargement of the left auricle but to thickening of the pericardium over it. It will be seen from the radiographs that a small heart shadow is not an essential feature of the condition; it must, however, be a "quiet heart."

It is suggested that the diagnosis of idiopathic pericarditis with effusion is nowadays untenable and that tuberculosis should be considered the likely ætiological factor in all stages of pericardial disease unless there is good reason for believing otherwise. Absence of constitutional signs and symptoms is in favour of this diagnosis and a sanguinous or straw-coloured lymphocytic exudate is confirmatory. At operation, tuberculous follicles and caseation may easily be missed on histological examination as the major portion of excised tissue may show only chronic collagenous, apparently non-specific, fibrous tissue. Paul White<sup>25</sup> found tuberculous tissue in a patient submitted to pericardectomy but only fibrosis in the pericardium at a later operation.

The presence of subacute tuberculosis of the pericardium is not a bar to operation for the relief of tamponade although such intervention must be very carefully timed.<sup>2</sup> Even where there is no such evidence, the post-operative period should be one of prolonged convalescence, and preferably sanatorial regime, owing to the possibility of lighting up latent infection. This occurred in two of our patients in the form of recurring pleural exudate and of synovitis in an elbow. The onset of tuberculous meningitis after such an operation has been reported.<sup>26</sup>

Cases 1, 2 and 3 are reported in full by Dr A. A. F. Peel in the *British Heart Journal*.<sup>27</sup> I have to thank him and Mr Bruce Dick for encouragement and help in preparing this paper.

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# ANÆSTHESIA FOR THE TUBERCULOUS PATIENT

By HERBERT H. PINKERTON

M.B., Ch.B., D.A., F.R.F.P.S.G., F.F.A.R.C.S.

I PROPOSE to confine my remarks almost entirely to the patient who suffers from tuberculous infection of the respiratory system, and who is to undergo some form of *thoracoplasty*, or a more radical *lobectomy* or *pneumonectomy*.

My own experience would indicate that the phthisical patient only rarely requires an operation for such common afflictions as those which haunt his more fortunate fellows, viz., appendicitis, hernia, perforated gastric ulcer, etc. On these rare occasions, the anæsthetist is called upon to supply an anæsthetic which is non-irritant to the lungs, adequate in potency, and which allows of an early return of the cough reflex and expectoration. Modern agents and methods—pentothal, cyclopropane, curare and local and spinal analgesia—provide an adequate choice.

## PRE-OPERATIVE

To-day the anæsthetist, rightly or wrongly, considers that he has an interest in the pre-operative and post-operative phases of the patient's treatment—pre-operatively, because he wishes his patient to be in the best shape for anæsthesia and operation, and post-operatively, because he may feel at least partly responsible for the onset of some complication and feel that it is his duty to share in the treatment. The case for thoracoplasty has been in bed often for months, with consequent severe reduction in *muscle-tone*, and on this account as well as on account of the disease of the lung, there is *diminished respiratory function*. In co-operation with the surgeon, the anæsthetist's first objective, therefore, is to seek some improvement in these before operation. Physiotherapy of an expert kind can do much to improve both muscle-tone and respiratory function, and strychnine, administered for a few days before and after operation, is helpful in raising muscle-tone, and as a result produces still further improvement in respiratory function. The morale of phthisical patients is good, and unlike ordinary patients, they do not fear the anæsthetic at all. As they have a considerable contact with patients who have already been operated upon, it is important that anæsthesia, being open to comment among such cases, should be as easy and comfortable as possible.

Read to the Tuberculosis Society of Scotland 18th June 1948.

## VITAL CAPACITY ESTIMATIONS

At Hairmyres Hospital, routine estimation of *vital capacity* is carried out by the physiotherapy staff, and some interesting though by no means conclusive points have eventuated. Two types of tracing have resulted—the *first* shows the initial improvement in vital capacity after physiotherapy, followed by a sharp fall after first stage thoracoplasty. The capacity gradually rises again under the guidance of the physiotherapist, to almost pre-operative level and falls again after the second stage. Again there is a gradual rise as the patient recovers. 103 out of 145 cases examined showed this type of tracing, and the results in this group were very good, the mortality being 3·8 per cent.

The *second* type of tracing showed a lower initial vital capacity, often in the region of 1500 c.c., and the usual fall took place after the first stage. In this type, however, little or no recovery in vital capacity took place, the figure remaining between 600 and 1000 c.c. This second type may be further subdivided into two classes—(1) the patients who in spite of a low vital capacity retained good control of their breath and managed the spirometer well, and (2) those who, in similar circumstances, had poor control of their breath and managed the spirometer badly. The experience and observation of the physiotherapist is the agency by which the subdivision is made, and experience shows that the former group will react well to the thoracoplasty and its stages, whereas the latter group appear doubtful risks for thoracoplasty and the postponement of a later stage should certainly be considered. The mortality rate in the last group is high, but it is worthy of special notice that, on the contrary, the mortality rate in the first subdivision is surprisingly low, considering the poor vital capacity. Two patients were lost out of 35 with a low vital capacity initially (1500 c.c.), and no recovery after the fall which followed the first stage of the thoracoplasty, subsequent stages being carried out while their capacity lay between 600 or 700 c.c., and 1000 or 1100 c.c. Many thoracic clinics prefer their patients to have a vital capacity of not less than 2000 c.c. before performing thoracoplasty, and even more clinics would consider 1000-1200 c.c. too low for operation. If these criteria were observed, 33 patients would have been denied the benefits of a successful thoracoplasty.

## ANÆSTHETIC TECHNIQUE

Considering the actual anæsthetic technique for thoracoplasty, general anæsthesia has been preferred. Remembering the importance of an immediate return of the *cough reflex* at the end of the operation—preferably on the table—premedication is light, no more than  $\frac{1}{2}$  gr. morphine and  $\frac{1}{160}$  gr. atropine, and the larynx is never cocaineised. Induction is carried out with pentothal intravenously, and anæsthesia is maintained with cyclopropane in a closed circuit. The patient is thus provided with a flexible anæsthetic, non-irritant to the lungs,

highly oxygenated, and allowing of a rapid return to consciousness. Many cases are equally well anæsthetised with gas-oxygen-trichloroethylene, but it is more difficult to maintain quiet respiration by this method. An endotracheal tube confers many advantages of which the most important is the facility offered for endotracheal suction at the close of the operation. The removal at this time of any sputum or secretions does much to prevent post-operative complications such as atelectasis and spread of the disease. An endotracheal tube is never introduced if there is any hint of tuberculosis of the larynx.

It should be noted that endotracheal suction may not always be sufficient to clear the sputum at the close and bronchoscopy may be required.

For some time, we have found curare to be valuable in first stage thoracoplasties—10-15 mg. are injected after anæsthesia is stabilised. The consequent relaxation of the shoulder-girdle allows the surgeon to make an excellent exposure of the upper ribs, and in addition, the curare prevents laryngeal spasm during periosteal stripping.

Many thoracic units prefer local analgesia, feeling that post-operative complications are reduced, and that it is easier to estimate the patient's reaction to the removal of the ribs, and so limit their number if distress appears. The method has obvious advantages as well as disadvantages, and its efficacy increases with experience in its execution.

### POST-OPERATIVE COMPLICATIONS

Whatever method is chosen, it is important that sequelæ should be minimal—the avoidance of post-operative atelectasis and spread of the disease is especially important in such patients and it is to this end that the various techniques are chosen.

The patient is encouraged to cough as soon as possible and morphia, judiciously used, relieves the pain engendered in the wound by the coughing. When a flushed face, dyspnoea and an elevation of temperature suggest some atelectasis, the physiotherapist is now doubly active. If her attentions are insufficient to clear the bronchial obstruction and response is sluggish, bronchoscopy under local analgesia should not be unduly delayed. It is normally carried out by the anæsthetist, who though not necessarily at fault, must feel that post-operative complications can be so easily caused by his own lack of skill and proper precaution.

Cardio-respiratory difficulties, which are probably due to disturbances following paradoxical respiration and mediastinal shift, are of mechanical origin. They are more common in younger patients in whom the anatomy is more mobile, than in older patients, who stand thoracoplasty remarkably well. As this mechanical distortion is probably in proportion to the number of ribs removed, it is possibly preferable to remove a lesser number of ribs at each stage rather than a greater. Modern anæsthesia is not hard on the patient, and an

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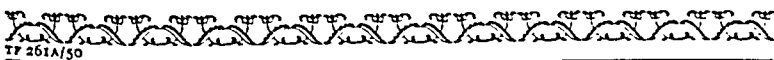
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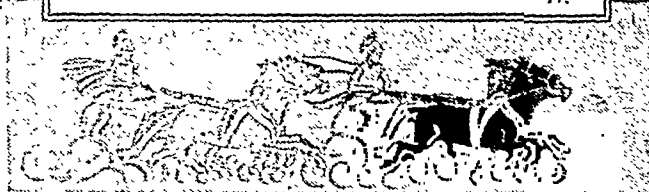
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Blood transfusion is rarely necessary, except occasionally before the second stage in the doubtful case. As there is no scientific method of assessing accurately a patient's fitness for the various stages, much reliance must still be placed on clinical judgment, and the views of the experienced physiotherapist are of much value.

### LOBECTOMY AND PNEUMONECTOMY

I would like to conclude with a few words on anæsthetic methods for lobectomy and pneumonectomy in tuberculosis. The actual agents are probably of less importance than the technique for coping with infective sputum and preventing spread to healthy lung. Pneumonectomy is less of a problem than lobectomy, as it is easier to isolate a whole lung than a lobe. The anatomical conformation of the main bronchi allows of reasonably easy endobronchial intubation of the left main bronchus when the right lung has to be removed, and of blocking of the left lung with a "bronchus-blocker" when the left lung has to be removed. The infective lung in each case is thus effectively isolated.

Tuberculosis, unlike bronchiectasis, usually involves an upper lobe and it is very difficult to isolate the diseased area. The most reasonable approach is to block the upper lobe bronchus by packing which is removed by the surgeon when the bronchus is isolated within the thorax. The method has had considerable success in the hands of those experienced in its use, the block being carried out under local analgesia. Posture to promote drainage, with suction through a wide-bore endotracheal tube is a compromise—in either event, bronchoscopy to clear secretions and sputum should conclude whatever technique is chosen.

# BASOPHILIC INFILTRATION IN THE NEUROHYPOPHYSIS

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THE basophil cells in the adenohypophysis are usually differentiated a little later than the acidophil cells, being first seen in the gland from a foetus three and a half to four months. Although Bailey maintains that there is no special arrangement of the different cells in the pituitary, yet the census of opinion is that they are more numerous at the periphery (Blair Bell, Vanderburgh, Fraser, Cooper, Biggart). Besides, round or polygonal basophilic cells are seen in the pars intermedia and may get scattered about in the neuroglial tissue of the pars nervosa (Rasmussen). Cushing attributes the occurrence of high blood pressure to the presence of these cells in the pars nervosa. The idea in this work is to ascertain the arrangement of these basophils and find out how far does this statement of Cushing's go?

## METHOD AND MATERIAL

Two hundred hypophyses were collected from the autopsy cases of the Neuropathology Department, Royal Infirmary, Edinburgh, without any selection. The glands were sagittally divided into two halves, fixed in Helly's fluid or in formalin, embedded in paraffin and sectioned serially at 6 micra. From every 166 sections two were mounted. One of the sections was stained with hæmatoxylin and eosin, while the other was kept for any specific stain. The stains used were eosin pyrol blue stain (Biggart) for the cytology and hæmatoxylin Ponceau fuchsin light green (Masson) for the connective tissue.

## RESULT AND DISCUSSION

The basophil cells together with the chromophobes are seen to occupy the peripheral zone of the pars distalis surrounding the acidophil cells which are grouped in the centre. This arrangement is fairly constant. With the advance of age and the occurrence of fibrosis in the gland a certain degree of distortion becomes visible. Occasionally masses of the basophil cells may become isolated and have been taken for neoplasms. The fact that these are regularly present and that they are not accompanied by symptoms of basophilism holds such a view as untenable.

Round and polygonal basophil cells are seen in the pars intermedia. Some of these basophil cells penetrate the connective tissue and infiltrate

the posterior lobe. Such basophilic infiltrations into the neurohypophysis are noted in 118 cases out of the 200 (*i.e.* 59 per cent.). The extent of the infiltration is variable. Usually, it is seen beginning in the centre of the zone of the lobe adjacent to the pars intermedia. In severe cases the infiltration extends along the inferior border of the pars nervosa and reach to the posterior pole of the gland (Fig.) Ten such cases were noticeable in the present study. A detailed investigation of these cases presents the following :—

TABLE

*Cases of Marked Basophilic Infiltration in Pars Nervosa*

Serial Number.	Laboratory Number.	Sex.	Age.	Blood Pressure.	Arteries.
1	1920	M.	57	Normal	Arteriosclerotic
2	2250	M.	36	"	Healthy
3	2198	M.	33	"	"
4	2358	M.	74	"	Arteriosclerotic
5	2381	F.	64	High	"
6	2831	F.	66	Normal	"
7	3131	F.	...	"	"
8	3191	M.	54	"	Healthy
9	3392	M.	53	"	Arteriosclerotic
10	3396	M.	74	"	Healthy

1. The infiltrations are more frequent in the males than in the females (7 : 3). On the other hand, pituitary basophilism is more common in females than males. This is corroborating evidence that such basophilic aggregations are not neoplastic.

2. The late decades of life are presumably the favourite age for their occurrence. Two cases only are at the ages of 33 and 36 years, while the rest are above 53 years of age.

3. Hypertension is only encountered in one case out of the ten. If the presence of these basophilic infiltrations were accompanied by rise of blood pressure, one would have expected to find them more or less constant in hypertension. This is not the case here. Again, other cases are seen in which the blood pressure is high while such basophilic infiltrations are absent. These findings show that there exists no actual correlation between the basophilia of the pars nervosa and hypertension.

4. Although arteriosclerotic changes are present in 6 cases, there are cases in which the arteries are healthy. Even in the cases with arteriosclerosis, the basophilic infiltrations cannot be considered responsible for the pathologic condition of the arteries because the latter can be attributed to old age. In favour of this argument are the two cases seen at the ages of 33 and 36 years. In these young cases, in spite of the presence of the basophilic infiltrations, the arteries are healthy.

Can these basophilic infiltrations be attributed to activity of the

pars intermedia? Fraser was the first to describe active and resting phases in the pars intermedia of the hypophysis of children. These basophilic infiltrations are particularly seen in old age, which is rather strange. The basophil cells are known to be responsible for the elaboration of the gonad stimulating hormones, but here the cases are seen in females at the age of the menopause. Therefore it is rather difficult to accept the view that hyperactivity of the pituitary is a reason for the presence of basophils in the pars nervosa.

### SUMMARY

1. The presence of basophilic infiltrations into the pars nervosa was seen in 59 per cent. of cases of autopsy material.
2. The view that some of these are neoplastic is discussed and rejected.
3. No relation exists between such basophilic infiltrations and hypertension.
4. This basophilic infiltration increases with age.

I wish to express my gratitude to Professor A. M. Drennan for his kind supervision and advice, and to Dr Blackwood for putting the material studied at my disposal.

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FIG.—Basophilic infiltration into the pars nervosa extending along the lower border to the posterior pole. E.P.B. stain—X.



FIG. 1.—Rathke's cleft cyst (R) separating pars nervosa from pars distalis along the whole sagittal plane. Ciliated cylindric epithelium is seen lining the wall.  $\times 40$ .

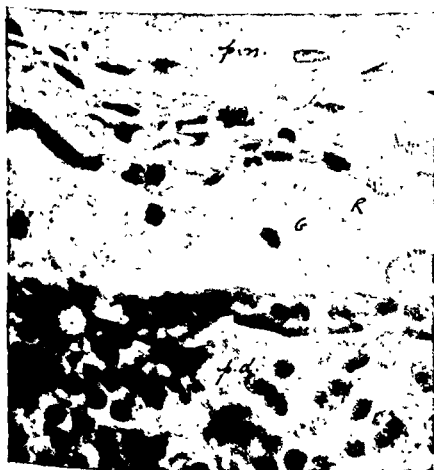


FIG. 2.—Large foam granular cells (G) derived from degenerating desquamated epithelial lining of a Rathke's cleft cyst (R). p.n. = pars nervosa. p.d. = pars distalis. H.E.  $\times 550$ .

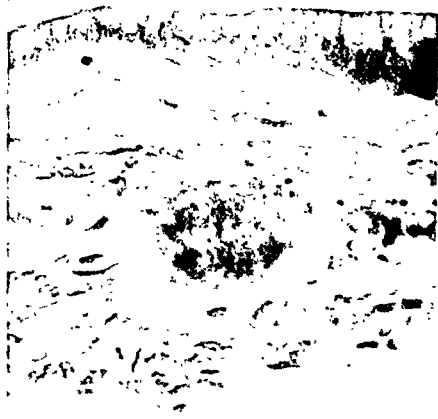


FIG. 3.—Wall of a Rathke's cleft cyst removed surgically from a patient. The highly cylindric mucous-secreting epithelial lining is evident. H.E.  $\times 350$ .



# RATHKE'S CLEFT AND ITS CYSTS

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It is generally known that the adenohypophysis develops from Rathke's pouch which is an invagination in the roof of the stomatodæum in front of the oral plate. The cells constituting the anterior aspect of the pouch proliferate with marked rapidity to form the pars distalis which becomes gradually vascularised. The dorsocaudal tip of the pouch develops into the pars intermedia. The residual lumen or "cleft" serves to separate these two portions of the gland and remains wide and definite during intrauterine life. After birth the lumen of the cleft is gradually obliterated except in a few small areas where acini containing colloid are obvious. A detailed study of the incidence and the histology of these cysts is felt necessary for the understanding of Rathke's cleft tumours.

## MATERIAL AND METHOD

Two hundred pituitary glands were collected from the autopsy cases of the Neuropathology Department, Royal Infirmary, Edinburgh, without any selection. As a routine, the glands were divided sagittally into two halves. Fixation was carried out in Helly's fluid, formalin or alcohol. Frozen sections were cut when necessary. The rest of the glands were embedded in paraffin. Serial sections were cut at 6 micra. Two sections were mounted at every 166th cutting. One section was stained with hæmatoxylin eosin and the other kept for further use. Sudan III and Mayer's mucicarmin stains were used to demonstrate fat and mucin respectively.

## RESULTS AND DISCUSSION

1. *Incidence of Rathke's Cleft Cysts.*—A distended cleft separating the pars distalis (anterior lobe) from the rest of the gland through the whole length of the sagittal plane (Fig. 1) has been noticeable in 26 cases out of the 200 cases (*i.e.* 13 per cent.).

Fraser attributed the distension of Rathke's cleft cysts, in childhood, to active stages in the intermediate lobe. In the present study there is no evidence to support this view. Cysts were detected in cases of 10, 10½ and 11 years of age and still the pars intermedia showed no evidence of proliferation or activity. These findings coincide with those of Cooper.

In adults the pars intermedia is reduced to a single layer of cells usually less than 10 micra thick. The cells present are predominantly



cuboidal or low columnar, but some round or polygonal basophilic cells are also seen in that lobe. According to Rasmussen (1930) these cells account for the great number of basophil cells which invade the pars nervosa. A detailed study of these 26 cases of distended Rathke's cysts and their correlation with such basophilic infiltrations of the neural lobe (see table) shows :

No invasion in	15 cases
Poor invasion in	2 cases
Moderate invasion in	8 cases
Marked invasion in	1 case

Taking the abundance of these basophil cells as a measure of the activity of the pars intermedia, one can deduce that, in adults, the distension of the cleft is not accompanied by proliferation of the intermediate lobe. On the contrary, it is obvious that the majority of the cases show atrophy of that part, probably due to pressure exerted by the distended cysts.

Brander is of the opinion that the cleft gets distended in cases of increased intracranial tension. Analysis of these 26 cases (see table) for intracranial findings shows :

Increased tension (various causes)	. . . . .	17 cases
Epilepsy	. . . . .	1 case
Brain atrophy	. . . . .	5 cases
No morbid changes	. . . . .	3 cases

Thus it is obvious that the cleft can be distended in cases with normal tension or even with cerebral atrophy. Again, the cleft is not constantly distended in other cases of brain tumours or hydrocephalus studied in which there has been marked rise in intracranial pressure.

2. *Structure of Rathke's Cleft Cysts*.—The cyst is lined in parts by tall columnar mucus-secreting epithelial cells possessing numerous delicate cilia. The nuclei are small, rounded, deeply stained and lie at the bases of the cells. Then ciliated epithelial cells are especially noticeable at the upper and posterior part of the cyst wall. They are invariably visible on serial sectioning. In other parts of the cyst wall, the epithelial lining has become compressed, flattened and has lost its cilia. The cysts usually contain one or more of the following elements :

- (a) Large foam cells with granular swollen cytoplasm and pyknotic excentric nuclei. Fat stains are negative, while the mucicarmine is positive indicating that the cells are derived from degenerating desquamated epithelium (Fig. 2).
- (b) Cholesterol crystals.
- (c) Mucinous material and granular debris with remains of disintegrated pyknotic nuclei.

The presence of ciliated cells in the human hypophysis was described by Bryant who claimed their existence in all freshly hardened human

hypophyses. Kiyono and Rasmussen (1929) found it only occasionally. Erdheim described the presence of ciliated epithelium lining the Rathke's cysts in man. Bailey stated that the cystic cavities lying between the distal and intermediate portions of the human hypophysis are lined with ciliated epithelial cells.

TABLE  
*Distended Rathke's Cleft*

Serial Number.	Laboratory Number.	Sex.	Intracranial Findings.	Basophilia in Pars Nervosa.
1	1673	M.	Brain atrophy	++
2	1932	F.	Hydrocephalus (cong. mem. blockage)	-
3	1955	M.	Infarction	++
4	2002	F.	Metastases, hydrocephalus	-
5	2066	M.	Pinealoma, hæmorrhage	++
6	2169	M.	Contusion	+
7	2237	F.	Epilepsy, no morbid change	-
8	2336	M.	Brain atrophy	++
9	2351	M.	No morbid changes	++
10	2460	M.	Chronic meningitis	-
11	2505	M.	Contusion, oedema	+
12	2533	F.	Fronto parietal atrophy (dis. scl.)	-
13	2593	F.	Glioblastoma (pons)	-
14	2741	F.	Spongioblastoma (chiasma)	-
15	2854	F.	No morbid changes	-
16	2858	M.	Glioblastoma	-
17	2887	M.	Traumatic abscess, meningitis	++
18	3016	M.	No morbid changes	-
19	3050	M.	Ependymoblastoma	-
20	3061	M.	Traumatic cyst	++
21	3161	M.	Brain atrophy	-
22	3182	M.	Arteriosclerosis, no cerebral lesions	-
23	3195	M.	Astrocytoma	-
24	3332	M.	Brain atrophy	++
25	3378	M.	Abscess	-
26	3382	M.	Traumatic cyst	+++

+ = poor; ++ = moderate; +++ = marked

The origin of these ciliated cells is difficult to ascertain.

Although Rathke, who first discovered the double origin of the hypophysis, believed that the pouch of mucous membrane assigned to the adenohypophysis was entodermal in origin, it was later shown by Goette, Balfour and Mihalkovics to be derived from the epithelium of the buccal cavity. A considerable controversy was raised when the development of the hypophysis was studied in various animals and three opinions existed at one time :

1. That it was entirely entodermal in origin (Hoffman, Ostroumoff, Prather).
2. That the entoderm made important contributions to the epithelial hypophysis (Kupfer, St Remy, Valenti, Smith, Atwell (1915), Miller, Bruni).
3. That the anterior lobe was entirely ectodermal (Reighard, Reighard and Mastl, Atwell (1918, 1926).

It is now generally accepted that the pouch is purely ectodermal. Thus the evidence for the participation of the entoderm in the formation of the human hypophysis is not sufficient to conclude that the origin of the ciliated cells is from this embryonal portion.

The embryologic studies of Duffy are unique in showing the hypophysial sac to be composed of stratified cylindric epithelium, most of which develops into the pars distalis, leaving a single layer of cylindric epithelium, often ciliated, to line the cleft. Rasmussen (1929) looks upon these ciliated cells as unusual differentiations of hypophysial tissues or as migrations of nasopharyngeal elements during early stage of development.

Thus, in spite of the unknown origin of these ciliated cells, it is ascertained that such cells are invariably found lining the Rathke's cleft cysts in the human hypophysis.

### SIGNIFICANCE

Rathke's cleft cysts may enlarge to such an extent as to give rise to symptoms. Clinically, they are identical with the hypophysial duct tumours (craniopharyngioma) arising from the lower group of epithelial rests at the root of the stalk. Histologically, these cysts form a separate entity from the epidermoid tumours.

In a pathological study of 47 cases, clinically diagnosed as epidermoid cysts, I have come across only one case of Rathke's cleft cyst.

CASE.—E. B., female, aged 14½ years, South African, admitted to Professor N. Dott's wards (R.I.E., No. 1337) complaining of deterioration of vision with a history of a blow on the eye two years previously; increase in weight for six months, polydipsia for two weeks. Examination revealed a blind left eye, light perception in right eye with primary optic atrophy on both sides, but more marked on the left. X-ray appearances were those of a flat and open sella. A radical extirpation of a supra pituitary cyst was performed. The cyst had no connection with the third ventricle and had a peculiarly thin wall.

Histologically, the cyst was lined by epithelium varying from cylindrical mucus-secreting type (Fig. 3) to immature epidermoid type. The nuclei were small, round, rich in chromatin and lying at the base of the cells. The cytoplasm was vacuolated simulating that of goblet cells. These highly cylindric epithelial cells were lying on a basis of collagen fibres. Some calcific deposits and areas of osteoid tissue were visible in the wall. The appearances were therefore identical with a Rathke's cleft cyst.

### SUMMARY

1. Distended Rathke's cleft cysts are found in 13 per cent. of hypophyses in examination of autopsy material.

2. No evidence was found to support the view that they are accompanied with stages of activity in the intermediate portion of the gland.

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3. Increased intracranial pressure plays no role in the distension of Rathke's cleft.

4. The presence of ciliated epithelium lining, at least in one part of the cyst wall, is ascertained by serial sectioning.

5. The differentiation of Rathke's cleft tumours from other congenital neoplasms of the hypophysis on histogenetic evidence is discussed and verified.

I wish to express my gratitude to Professor A. M. Drennan for his advice on and supervision of the work. My thanks are due to Professor N. Dott who very kindly placed all his clinical records at my disposal and gave me permission to study his cases. The microphotographs are the skilled work of Mr T. C. Dodds.

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# FŒTAL CELL ADENOMATA OF THE HYPOPHYSIS CEREBRI

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A STUDY of the adenomata of the human hypophysis and their classification on a histo-genetic basis reveals a group of tumours arising from embryonic cells. These neoplasms form a special entity with a characteristic morphological picture which needs to be dealt with in detail.

## MATERIAL AND METHOD

The material studied consisted of two groups. The first group comprised 105 cases of hypophysial chromophobe adenomata removed surgically. As a routine, in the vast majority of these cases, two biopsies were taken. One specimen was fixed in 15 per cent. formalin and the other was put in Regaud's fluid. Very few cases were fixed either in formalin or in Helly's fluid. The tissues were embedded in paraffin. Sections at 6 micra were cut, mounted and stained with hæmatoxylin and eosin. For the cytology and the study of the granules, spare sections were specifically stained by one or more of the following stains.

1. Eosin pyrol blue (Biggart).
2. Mann's methyl blue eosin (Carleton).

Other stains used were: Van Gieson for collagen, Laidlaw, Wilder and Gordon-Sweet for reticulum. As the constancy of the histologic type of the hypophysial adenomata is striking (Schintker and others), I felt justified in studying at least three or four sections from each case.

The second group comprised 200 hypophyses collected without selection from the autopsies of the Neuropathology Department of the Royal Infirmary, Edinburgh. These were fixed either in formalin or in Helly's fluid, embedded in paraffin and cut serially at 6 micra. Two sections were mounted from every 166th plane. One of the sections was stained with hæmatoxylin and eosin and the other with the specific stain required.

## RESULT

There are no particular naked-eye features to distinguish the various types of the chromophobe adenomata from one another. Comparatively the tumour under consideration is less vascular than the ordinary type of the chromophobe adenomata. Again the tumour does not exhibit any special predilection to extra-sellar extension or any particular behaviour different to the chief cell type.

*Histologic Appearance.*—Apart from the well-known chromophobe adenomata which arise from the chief cells or "Hauptzellen" of

Stieda and which present sinusoidal, papillary or diffuse patterns, there is another type of tumour composed of highly columnar or cylindrical cells. The cytoplasm appears like ground glass in the sections stained with hæmatoxylin and eosin. Specific stains show a delicate, finely granular, pale staining, polychromatic cytoplasm. These cells have oval, excentric nuclei rich in chromatin which is evenly distributed. The tumour pattern is papilliferous (Fig. 1). The cells are arranged radially about the blood channels and the connective tissue cores like palisades. The nuclei are visible in the part of the cell lying away from the blood vessels (Fig. 2). The papillary appearance of the tumour is especially noticeable at the periphery. Proceeding inwards into the centre of the tumour, the papillæ gradually become approximated and finally compressed as the tumour grows. This gives the central portions of the tumour a compact appearance. Consequently, the cell aggregations resemble "rosette" forms (Fig. 3). The transition of the papillary arrangement into a compact trabecular one can be well demonstrated by staining for connective tissue or by impregnation with silver for the reticulin in the stroma (Figs. 4 and 5). The stroma of these adenomata is usually delicate and of a moderate vascularity (only 13 per cent. are highly vascular). A few mitotic figures can be seen scattered in the tumour.

Colloid cysts are occasionally visible in these tumours, but to a lesser degree than in the chief cell adenomata. The actual figures are 13.3 and 17.7 per cent. respectively.

*The Incidence.*—Out of the 105 chromophobe adenomata 38 tumours contained these highly columnar undifferentiated cells. Fifteen cases were totally composed of these cells, while the rest were a mixture of chief and foetal cells (22 cases) for transitional and foetal cells (1 case).

## DISCUSSION

Hannover was the first to describe two kinds of epithelial cells in the anterior lobe of the hypophysis, yet little attention was bestowed upon his findings and the credit was given to Flesch who applied the terms "chromophiles" and "chromophobes." Schoeneman using hæmalum eosin stain was able to differentiate the chromophiles into "oxyphilic" and "cyanophilic" cells. The "Kernhaufen" or nuclear heaps described by Rogowitch in protoplasmic masses were identified by Stieda to be actual cells with boundaries. The term "Hauptzellen" = chief cells, was applied to them and their nature was considered to be chromophobic.

Another type of cell, namely the "foetal cell," was described by Lowenstein, but little attention was paid to it. These are the "undifferentiated epithelial cells" of Cooper which first appear in the gland and soon differentiate into the other types of cells.

The study of the autopsy material shows that groups of these cells exist in the pars distalis at all ages. They are commonly situated in



the peripheral zone of the anterior lobe, especially at its lower and posterior part near the cleft. The cells are cylindrical and possess a deeply stained nucleus with a fair amount of evenly distributed chromatin. The cytoplasm is abundant and faintly stained with hæmatoxylin and eosin stain and is faintly polychromatic with the eosin pyrol blue stain. The cells are arranged in tubules or cords which lie against blood capillaries on one side and line tubular cavities on the opposite side. Solid masses of these cells are seen but these are nothing but compressed tubules grouped together. In other words, they are not an aberrant alveolar arrangement as may be understood from the description of Kraus (1926). When viewed in transverse section the cells are usually arranged radially around the capillaries, in a palisade pattern (Fig. 6). The nuclei lie in the part of the cell remote from the blood channel. Therefore, these cells, for all morphological purposes, are identical with the cells constituting the group of adenomata under present investigation. Not only that, but also

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FIG. 1.—Papilliferous pattern of the foetal cell adenomata of hypophysis. H.E.×80.

FIG. 2.—Perivascular palisade arrangement of the cylindric foetal cells in the tumour. The nuclei lie away from the capillaries. H.E.×150.

FIG. 3.—“Rosette” forms in a compact central portion of a foetal cell adenoma (R, R). Colloid cysts are visible (C.V.). H.E.×160.

FIG. 4.—Foetal cell adenoma showing the reticulum fibrils of the stroma and the typical perivascular papillary arrangement. Silver impregnation. ×160.

FIG. 5.—Trabecular arrangement of a compact part of the foetal cell adenoma. Silver impregnation. ×160.

FIG. 6.—Foetal cells (*f*) showing the characteristic pattern in the pars distalis of a hypophysis. H.E.×80.

FIG. 7.—Subclinical hypophysial adenomata in the pars distalis. A = foetal cell type with a papillary pattern. B = chief cell type with a diffuse pattern. H.E.×40.

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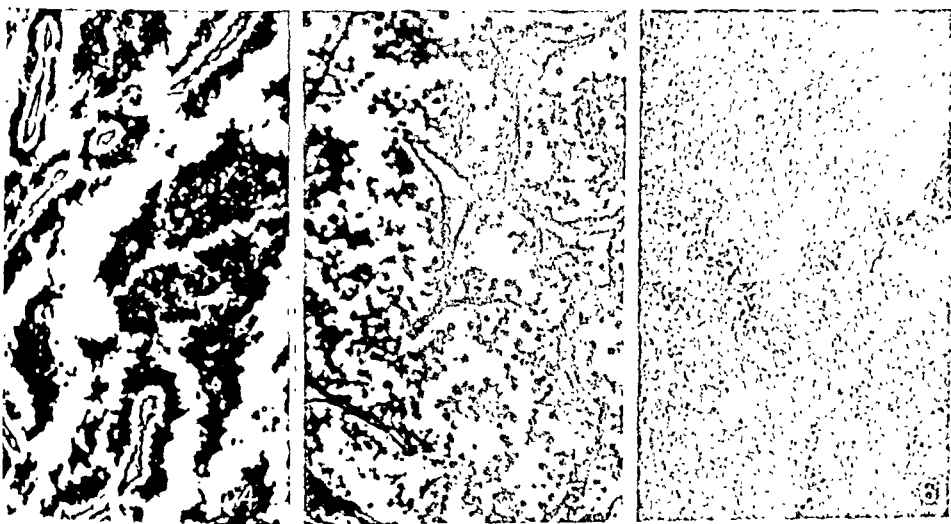
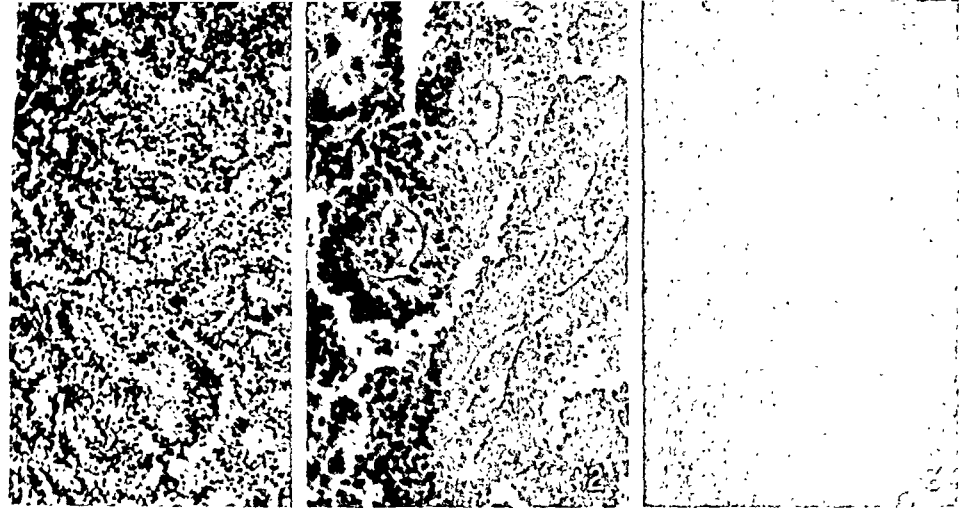
among 24 subclinical chromophobe adenomata discovered accidentally in these 200 autopsy cases, 9 proved to consist of these foetal cells. Fig. 7 illustrates clearly the structural differences between the chief and the foetal cell adenomata as seen in one case.

Shapiro described an incidental observation of a foetal adenoma in a patient with peptic ulcer. Kraus (1945) in a recent contribution to the neoplastic diseases of the hypophysis recognises the foetal cell adenomata as a separate entity.

### SIGNIFICANCE

The importance of this recognition of the foetal cell adenomata becomes obvious when the duration of the chromophobic adenomata is studied in correlation with the cell type (table).

The majority of the foetal cell adenomata (10 out of 15) or tumours containing foetal cells (16 out of 23) have a duration period less than five years. Again, about 55 per cent. of the tumours with a duration period less than one year are of the foetal cell type. The incidence of the foetal cells in the hypophysial chromophobe adenomata that





have a duration period above three years diminishes to nearly one third of these cases.

TABLE

*Duration of the Various Types of Chromophobe Adenomata*

Duration.	Number of Cases containing				Percentage of Cases with Fœtal Cells.
	Fœtal Cells.	Other Cells.	Mixture.	Total.	
Up to 1 year . . .	4	9	7	20	55.0 per cent.
" 2 years . . .	1	10	3	14	28.5 "
" 3 " . . .	3	6	3	12	50.0 "
" 4 " . . .	1	3	1	7	28.5 "
" 5 " . . .	1	7	2	10	30.0 "
" 10 " . . .	3	15	2	20	25.0 "
Above 10 years . . .	1	10	3	14	28.5 "
Unavailable . . .	1	5	2	8	...
Total . . .	15	67	23	105	

## SUMMARY

1. A study of the foetal cells of the adeno-hypophysis is given and its detection in the gland at various ages is mentioned.
2. Subclinical adenomata arising from these cells are detected.
3. The recognition of a group of clinical adenomata histo-genetically related to these embryonic cells is ascertained and the microscopic picture is fully described with illustrations.
4. The shorter duration period of these foetal cell adenomata compared to the chief cell tumours is referred to.

I have to thank Professor A. M. Drennan for his kind supervision and advice and to record my indebtedness to Colonel Harvey and Dr Lees of the Royal College of Physicians Laboratory (Edinburgh) for putting this collection of material at my disposal. Professor N. Dott very kindly gave me permission to study his cases. Thanks are due to Mr T. C. Dodds for the illustrations.

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# CANCER AND THE CO-ORDINATION OF CONTACT AND INDUCTIVE INFLUENCES

By MAURICE COPISAROW, D.Sc.

RECENT work on the inductive activity of chemical carcinogens links their function with that of radium emanations, X-rays and short electro-magnetic waves and provides a logical basis for the uniform metabolism characterising malignant growth. Thus, the identification of carcinogenic substances on the basis of chemiluminescence emitted during hydroxylation,<sup>1</sup> rather than their constitution or reactive groupings, emphasises the significance of the inductive aspect of the problem. This finds a theoretical background in the concept of a regional high intensity of electrons within the molecule of the carcinogenic polycyclic hydrocarbons.<sup>2</sup> Carcinogenesis is viewed here as being due to an interaction between the high electron density and some protein molecule, by which a quantal change in the molecule is facilitated. The suggested modulated denaturation of nucleo-proteins by ultra-violet light of varying wave-lengths in presence of photosensitising porphyrins,<sup>3</sup> and the formation of free radicals, hydroxylated and polymerised products, by the action of ionising radiations upon organic substances in the presence of water<sup>4</sup> both further stress the interdependence between the contact and inductive aspects of carcinogenic reactions.

The significance of these reactions becomes more apparent when considered in relation to enzymic systems, the prolonged inhibition of which is basic to the cancer problem.<sup>5</sup> Only as enzymic complexes can proteins, vitamins, etc., participate in the various metabolic changes. Likewise, an association with enzymic systems is essential for carcinogenic agents to become operative.<sup>6</sup> This association appears to take place at the most reactive point, a region of high electron density, within the carcinogenic molecule, subsequent hydroxylation being effected at some less sensitive part of the substance.<sup>7</sup> Thus, a carcinogenic compound may be defined as one which, during its metabolism, evolves sufficient energy in the form of radiation of a particular wave-length band.<sup>1</sup> Such a co-ordination of carcinogenic influences on a common inductive basis constitutes an important addition to our knowledge. This very fact, however, accentuates the present lack of differentiation between pathogenic and beneficial radiations.

A more complex and crucial aspect of the problem is to be found in the inter-relation between the various energy forms and levels within the organism. Here, radiations from external, mainly solar sources, are converted into chemical energy and accumulated in a vast series of organic forms. The metabolism of these forms is brought about by a chain of physico-chemical reactions accompanied by induc-

tive emissions over a wide spectrum range. All these metabolic emissions are due to enzymic activity, mainly the oxidase-dehydrogenase system, and include electrical phenomena and radiations in the visible and ultra-violet spectrum range.<sup>5</sup> The distribution and function of these enzymes, and consequently their inductive emissions, vary with the organism and type of organ, and are subject to such influences as season, excitation, availability of oxygen, etc. This applies to both bioluminescence and mitogenetic radiation, and such differences in wave-length as recorded by Gurwitsch,<sup>8</sup> and Reiter and Gabor<sup>9</sup> clearly emphasise this point and certainly do not imply, as favoured by some critics,<sup>10</sup> sheer experimental discrepancies.

It may therefore be assumed that metabolic radiations exhibited by oxidation enzymes from various sources, differ but little once these enzymes are removed from their active cellular environment—be it a single cell or group of cells—as is found in the assimilation of cellular matter by another organism. In the living cell, however, both the wave-length and intensity of radiation, are subject to the controlling influence of the electric field surrounding such pulsating entities. Such differentiation leads to conditions under which the inductive effects between various organic forms are often antagonistic to one another. Thus, the well-defined metabolic radiation of one organism may be influenced by that of another, the weaker becoming the receptor or indicator. Biological tests for ultra-violet (mitogenetic) radiation as well as its inhibition in the cases of parasitic infection (syphilis, tuberculosis, etc.) are instances of such interference.<sup>11</sup> Here is found the solution to the apparent contradiction of facts, namely, cell mitosis being adversely influenced by either radiations from other organisms or enzymic inhibition within the organism and consequent suppression of radiation in the cells undergoing mitosis, as in the case of cancer.<sup>12</sup> Carcinogens are cumulative in their action, and the initial fatigue-like damping of normal metabolic radiations is followed in course of time by complete inhibition. The interference of pathogenic radiations with metabolic emissions may perhaps be compared with the interference of radio-waves, and radio technique may provide some guidance in this respect. Again, the conditions under which such radiations penetrate the electric field around the cell may perhaps be correlated to certain astronomical and geo-physical phenomena.

This co-ordination of all contact and inductive reactions and their merging within the orbit of enzymic activity represents an extension of earlier work on the bio-chemical factors and control of cancer.<sup>13</sup> Malignant growth was recognised as a complex deficiency disease, in which the characteristically distorted metabolism is founded on a protracted inhibition of relevant enzymic systems. The suggested control attempted to restore the enzymic and especially the sulphhydryl-sulphoxide equilibrium. Carcinogenic influences were countered here by diet and culinary adjustments, administration of active enzymic vitamin systems and suitable sulphoxide compounds. The inhibit

effect of cysteine hydrochloride and d-l-serine upon both the photodynamic and carcinogenic activity of 3:4 benzpyrene<sup>14</sup> shows that the proposed treatment is applicable to both the contact and inductive phases of cancer.

In general, all functional and structural aspects of metabolism are controlled by the complementary action of contact and inductive influences. Thus the distorted enzyme—hormone equilibrium, the induced gene mutations and the chromosomal changes provide a common basis for all forms of cancer.

### SUMMARY

Recent work on chemiluminescence, ionising radiations, photosensitising substances and regional electron densities within the molecule reveals the existence of an inductive phase in all contact carcinogens and therefore provides a common basis for carcinogenic influences.

Carcinogens are characterised by their distorting effect upon the enzymic equilibrium of the organism. They suppress the enzymes which under normal conditions are responsible for inductive emissions over a wide spectrum range. Thus, carcinogenic action may be viewed as the penetration of the electric field surrounding the cell or as the suppression of metabolic inductive activity by pathogenic radiations.

It would, therefore, appear that anti-carcinogenic measures must be directed to the restoration of the normal enzymic equilibrium as already outlined in earlier papers.

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## DIABETES MELLITUS—A REVISED CONCEPTION OF ITS STANDARDISATION

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THE number of diabetics is increasing every year. The increased span of life of the diabetic—at least three times as long as a quarter of a century ago—the propagation of individuals with a diabetic heredity, as well as the more frequent diagnosis of the mild type of the disease, have all led to an increase in the total number. At the present rate of increase we shall, within the next ten to twenty years, be presented with a social problem that must eventually be boldly faced.

"Before 1914, both von Noorden and I each saw approximately two-thirds of our patients dying of diabetic coma, and even with the introduction of the theory of under-nutrition by F. M. Allen this mortality was only lowered to 40 per cent. by 1922." This was the experience of E. P. Joslin in America. The isolation of insulin in 1922 immediately lowered the appallingly high mortality rate of those diabetics who could not be standardised on diet alone. The hypothesis that diabetes was primarily due to defective production of a pancreatic hormone had been suggested by some investigators. Banting and Best brilliantly provided the proof and converted hypothesis into fact. Accordingly, it was hoped that simple replacement therapy would solve the diabetic problem. The aim of treatment was to imitate physiology as closely as was humanly possible. In order to achieve this, the common practice at first was the advocacy of a low carbohydrate diet; insulin was used unsparingly, if necessary, to lower the blood sugar as closely as possible to normal levels throughout the twenty-four hours and to prevent anything but the slightest trace of glycosuria. The low carbohydrate diet therapy has become universally obsolete. Insulin, however, is still used to keep the urine sugar-free as far as possible and so lower the blood sugar to strictly normal limits. A period of hospitalisation is advocated by most physicians, *e.g.* three to four weeks by Sir Edmund Spriggs in *The Practitioner* of May 1939. In some cases the patient is taught to construct his diet from charts showing the composition and caloric values of various foods. I show those who are not able to undertake the calculations needed to n<sup>c</sup>



patients have not had to take advantage of this. Similarly, no patient has suffered a hypoglycæmic attack, nor would this be expected in view of the hyperglycæmia permitted. A few examples from records of the present clinic may help to show the type of check-up that is made. It will be seen that blood sugars are recorded for the sake of completing the clinical records according to modern standards, but it must be re-emphasised that treatment is not dictated by the figures obtained. At the same time treatment is not dictated by the amount of urine sugar excreted in twenty-four hours. Even though a patient excretes an appreciable amount of glucose in his urine in twenty-four hours, if he has no acetonuria, no symptoms, no loss of weight or complications and is able to do his work, his metabolism is considered to show a positive balance in terms of health and efficiency. If this is attained on diet alone, no insulin is required to lower the blood sugar and prevent the glycosuria. On the other hand, a patient who excretes only a small amount of glucose, but who continues to lose weight and complains of symptoms, is not well balanced but will require some insulin. For the purpose of the clinic, urine sugar is only recorded as trace, 1 plus, 2 plus or 3 plus. The indication for giving insulin is a simple one, namely when a diet adapted to the individual's needs does not achieve the desired standards of efficiency, so that he still does not feel well or fails to maintain the weight considered necessary or presents signs of acidosis or complications. The amount of insulin to be administered remains a matter of trial and error in each individual patient and is guided by the particular clinical picture of the patient concerned and not by his blood sugar level alone. Scott and Dotti wrote in 1932 that despite the multiplicity of papers on insulin research our knowledge of the deeper significance of insulin is still disappointing. About its pharmacodynamics we still remain largely ignorant up to the present day. "The most important reference books and current texts on the subject of diabetics do not provide the answers. Although every conceivable aspect of insulin is summarised and reviewed, we have been unable to ascertain from the mass of material any formula by which the physician can be guided." This is the conclusion of Collens and Boas in their recent textbook, *The Modern Treatment of Diabetes Mellitus*. The severity of a diabetic cannot be expressed in terms of insulin required, for this varies according to the individual variation of insulin sensitivity. Himsworth has devised an insulin-glucose sensitivity test and he goes so far as to state on the basis of this test that "insulin sensitive diabetics tend to be younger, thin, and to have a normal blood pressure and healthy arteries, in them the disease is sudden and severe at onset; they easily develop ketosis and react to a slight excess of insulin with a hypoglycæmic attack. The insulin-insensitive diabetics, on the other hand, tend to be older, obese, to have hypertension and to exhibit arteriosclerosis; in them the onset of the disease is insidious. They rarely develop ketosis and can tolerate over-dosage of insulin without showing

symptoms of hypoglycaemia." From the practical standpoint, we sub-divide diabetics into three main types:—

- (1) Mild—standardised on diet alone.
- (2) Moderate—standardised on diet and insulin.
- (3) Severe—difficult to standardise on diet and insulin.

The latter we have encountered mainly among the younger diabetics who appear to resemble closely Himsworth's insulin-sensitive type.

A few examples from present clinic. There is nothing of especial interest about the figures shown below. They are inserted merely to indicate the type of supervision considered necessary and it must be emphasised that it is carried out at a single session. This time-saving is an important factor from the point of view of an employee.

1. Miss M., aged 24 years. History of diabetes of twelve years' duration including 9 known diabetic comas. At one time she had been completely hospitalised for a period of three years. She had recently left hospital with the advice to inject 20 units sol. insulin t.d.s. She said she "did not understand" her diet as it had been changed so repeatedly. She complained of not feeling well. On examination, she was obviously below average weight and her breath smelt strongly of acetone. She had never had a job and was unable even to go out alone.

Date.	Urine Sugar.	Acetone.	Blood Sugar Fast: mgm./100 c.c.	Weight St. Lbs.	Treatment.		Remarks.
					Diet.	Insulin.	
26. 8.47	+++	++	285	7 10½	Standard diet +200 cal.	Sol. }25 u.a.m. insulin }15 u.p.m.	Complaining of lassitude, headaches, some thirst.
2. 9.47	++	Nil	200	7 11½	Standard diet +200 cal.	Sol. }25 u.a.m. insulin }15 u.p.m.	Feeling better.
16. 9.47	++	Nil	194	8 0	Standard diet +300 cal.	Sol. }25 u.a.m. insulin }25 u.p.m.	Diet and insulin increased.
23. 9.47	+	Nil	170	8 2	Standard diet +300 cal.	Sol. }20 u.a.m. insulin }25 u.p.m.	Improving.
30. 9.47	+	Nil	165	8 3	Standard diet +300 cal.	Sol. }15 u.a.m. insulin }20 u.p.m.	Improving.
7.10.47	Trace	Nil	155	8 6½	Standard diet +300 cal.	Sol. }15 u.a.m. insulin }15 u.p.m.	Further insulin reduction made.
14.10.47	++	Nil	170	8 6½	Standard diet +300 cal.	Sol. }15 u.a.m. insulin }15 u.p.m.	Feels and looks well.
28.10.47	++	Nil	170	8 6½	Standard diet +300 cal.	Sol. }15 u.a.m. insulin }15 u.p.m.	Feels and looks well.
7.11.47	+	Nil	160	8 4	Standard diet +300 cal.	Sol. }20 u.a.m. insulin }20 u.p.m.	No gain in weight for three weeks. Diet and insulin increased.
25.11.47	+++	Nil	195	8 7½	Standard diet +500 cal.	Sol. }20 u.a.m. insulin }20 u.p.m.	Patient pleased with extra carbohydrate.
16.12.47	+++	Nil	168	8 6	Standard diet +500 cal.	Sol. }20 u.a.m. insulin }20 u.p.m.	Reports that she has a job.
6. 1.48	++	Nil	200	8 8	Standard diet +500 cal.	Sol. }20 u.a.m. insulin }20 u.p.m.	Condition maintained.
27. 1.48	+	Nil	170	8 12½	Standard diet +500 cal.	Sol. }20 u.a.m. insulin }20 u.p.m.	Condition maintained at this weight.

2. Mrs B., aged 43 years. Referred from doctor with past history of severe diabetes.

Date.	Urine Sugar.	Acetone.	Blood Sugar Fasting mgm./per cent.	Weight. St. Lbs.	Treatment.		Remarks.
					Diet.	Insulin.	
9.10.45	++	Nil	210	11 12	Standard diet	P.Z.I. 34 u.mane.	Complains of headaches and giddiness. B.P. 180/125.
16.10.45	++	Nil	170	11 8½	Standard diet	P.Z.I. 30 u.mane.	Quite well, B.P. unchanged.
23.10.45	++	Nil	175	11 9	Standard diet	P.Z.I. 30 u.mane.	Occasional symptoms thought to be consistent with hypertension.
6.11.45	++	Nil	190	11 13	Standard diet	P.Z.I. 26 u.mane.	Diabetes under satisfactory control.
27.11.45	++	Nil	200	11 13	Standard diet	P.Z.I. 26 u.mane.	Diabetes under satisfactory control.
4.12.45	++	Nil	170	11 13	Standard diet	P.Z.I. 26 u.mane.	Diabetes under satisfactory control.
8. 1.46	+	Nil	190	11 13½	Standard diet	P.Z.I. 26 u.mane.	B.P. 195/115.
22. 1.46	+	Nil	220	12 1½	Standard diet	P.Z.I. 26 u.mane.	Mild bronchitis, some dyspnoea and headaches.
12. 2.46	+	Nil	195	12 1	Standard diet	P.Z.I. 22 u.mane.	Improved again.
5. 3.46	+	Nil	166	11 13½	Standard diet	P.Z.I. 22 u.mane.	Condition unchanged.
19. 3.46	+	Nil	200	12 0	Standard diet	P.Z.I. 22 u.mane.	Condition unchanged.
9. 4.46	+	Nil	188	11 13½	Standard diet	P.Z.I. 18 u.mane.	Condition unchanged.
30. 4.46	Trace	Nil	173	12 0	Standard diet	P.Z.I. 16 u.mane.	Condition unchanged.
From this time patient has been seen at intervals of four and five weeks. No change has had to be made in diet or insulin.							
Latest Attendance							
6. 2.48	+	Nil	205	12 0½	Standard diet	P.Z.I. 16 u.mane.	B.P. 190/115.

3. Miss H., aged 28 years. Referred by doctor suffering from loss of weight and thirst. Glycosuria and diabetic blood sugar curve found.

Date.	Urine Sugar.	Acetone.	Blood Sugar mgm./100 c.c.	Weight. St. Lbs.	Treatment.		Remarks.
					Diet.	Insulin.	
22. 4.47	++	+	370	7 11½	Standard diet +150 cal.	{P.Z.I. 20 u.mane. {S.I. 20 u.mane.	...
29. 4.47	++	Trace	240	7 11½	Standard diet +150 cal.	{P.Z.I. 20 u.mane. {S.I. 20 u.mane.	...
13. 5.47	++	Nil	220	7 12½	Standard diet +150 cal.	{P.Z.I. 20 u.mane. {S.I. 20 u.mane.	...
10. 6.47	++	Nil	200	7 9½	Standard diet +150 cal.	{P.Z.I. 20 u.mane. {S.I. 20 u.mane.	...
24. 6.47	++	Nil	230	7 8	Standard diet +500 cal.	{P.Z.I. 25 u.mane. {S.I. 25 u.mane.	...
1. 7.47	Trace	Nil	155	7 9	Standard diet +500 cal.	{P.Z.I. 25 u.mane. {S.I. 25 u.mane.	...
29. 7.47	+	Nil	180	7 11½	Standard diet +500 cal.	{P.Z.I. 20 u.mane. {S.I. 20 u.mane.	...
10. 9.47	+	Nil	180	7 11½	Standard diet +500 cal.	{P.Z.I. 25 u.mane. {S.I. 20 u.mane.	...
30. 9.47	+++	Nil	200	7 13½	Standard diet +500 cal.	{P.Z.I. 25 u.mane. {S.I. 20 u.mane.	...
23.10.47	+	Nil	164	7 13½	Standard diet +600 cal.	{P.Z.I. 25 u.mane. {S.I. 20 u.mane.	...
4.11.47	++	Nil	185	7 13½	Standard diet +600 cal.	{P.Z.I. 25 u.mane. {S.I. 20 u.mane.	...
11.11.47	++	Nil	180	7 13½	Standard diet +600 cal.	{P.Z.I. 25 u.mane. {S.I. 20 u.mane.	...
2.12.47	+++	Nil	185	8 2	Standard diet +600 cal.	{P.Z.I. 25 u.mane. {S.I. 20 u.mane.	...
23.12.47	+	Nil	175	8 0	Standard diet +600 cal.	{P.Z.I. 25 u.mane. {S.I. 25 u.mane.	...
6. 1.48	++	Nil	170	8 0	Standard diet +600 cal.	{P.Z.I. 25 u.mane. {S.I. 25 u.mane.	...

In his follow-up visits, if the patient does not have enough to eat, moderate additions are made to his diet. Unjustifiable loss of weight in a standardised diabetic is immediately investigated for extra-diabetic causes. The diabetic is just as prone to malignant disease as anyone else. Continual alertness to detect early phthisis in a curable stage demands that every cough be thoroughly investigated, as the condition responds quite well if the diabetes is adequately controlled. In the event of active complications the diabetes is more vigorously treated until the condition is halted or eradicated, and insulin is either given or increased in dosage even though not required for standardisation purposes. For instance, cases of pruritus vulvæ, so common and often the only symptom of the menopausal diabetic, respond rapidly to this additional insulin which can be later withdrawn. Retinitis and cataract are more rigorously treated in consultation with the eye specialist. Prophylaxis against gangrene is strongly urged in cases of corns and calluses, and patients referred for careful chiropodist attention. In such conditions as boils and colds the insulin dosage is increased and the patient seen again in one week.

Many gaps remain to be filled in our knowledge of the causative factors of diabetes and its associated diseases. Agreement has not been reached with regard to the pathological changes to be found in the pancreas and their significance from the aetiological standpoint. In actual fact, there is no evidence at present as to whether insulin secretion in diabetic patients is decreased, unaffected or increased in amount; there is no doubt, however, that it is less effective than normally. Recent work suggests that diabetes mellitus is not simply a disease of the pancreas. The work of Houssay and his associates in South America since 1937, followed by that of Young, has gone far to establish the view, at any rate in the experimental animal, that a diabetogenic hormone is produced in the anterior pituitary gland which is antagonistic in its action to that of insulin. Himsworth asserts that "the anti-insulin factor of pituitary extracts has the property required to produce the state of insensitivity to insulin characteristic of one type of diabetic patient, and it was found that after injection of such an extract into a normal animal the previously normal insulin-glucose curve was changed to an abnormal insulin-insensitive type." Young was able to induce hydropic degeneration of the islands of Langerhans in animals injected daily with large doses of anterior pituitary extract. Haist, Campbell and Best in repeating the experiments of Young observed that the production of permanent diabetes by the injection of large doses of anterior pituitary extract is accompanied by a marked depression of the insulin content of the pancreas. When, however, the animals were injected with anterior pituitary extract at the same time that they were either starved or fat fed or given insulin, they were able to prevent the development of diabetes and the insulin content of the pancreas was not seriously affected. Hydropic degeneration of the islands of Langerhans had been produced formerly by

Allen in the remainder of the pancreas after partial pancreatectomy in dogs. When seven-eighths of the pancreas was removed, these dogs were overfed and developed diabetes. He conceived the theory that degeneration of the islands resulted from their exhaustion through overwork. In the same way it has been suggested that the prolonged hyperglycæmia induced by the repeated injections of anterior pituitary extract causes the cells of the islets of Langerhans to undergo functional exhaustion and degeneration and that control of the hyperglycæmia before the pancreatic changes have advanced too far, can prevent the development of permanent diabetes. Further, it has been suggested that this might have important clinical implications. In practice, we have encountered quite a number of diabetics, usually of the later age-groups, who in spite of a persistently high blood sugar level have required gradually diminishing insulin doses for their standardisation as the years elapsed. Collens and Boas are of the opinion that resting the pancreas by creating smaller demands for endogenous insulin production appears to be only a transient form of relief.

Hyperglycæmia has always been suspect of exerting a noxious influence in some way or other. In the past it has been considered responsible at one time or another for certain of the diabetic complications. For example, it was thought that the increased sugar content of the blood and tissues seen in diabetic patients favoured the growth of bacteria, particularly staphylococci. Present-day opinion does not favour this explanation. There is by no means agreement that an increase of sugar in the blood predisposes to diseases of the skin. It seems certain that diabetic neuropathy is not the direct result of hyperglycæmia or ketosis, it may be seen in patients whose diabetes is well controlled by diet and insulin, whereas other patients who were free of neurological signs before treatment have developed symptoms and signs shortly after treatment has been started. The factors involved in bringing about certain degenerative changes in the diabetic are far from being elucidated. There has frequently been a tendency to fasten a greater part of the blame on to the diabetes or even on to the hyperglycæmia *per se*. Wilder, although recognising the great incidence of arteriosclerosis in diabetes and the importance of its treatment as a complication of diabetes, doubts that the vascular lesions are due solely to diabetes. Retinal changes occur predominantly in adult diabetics who have hypertension but may also be present in the juvenile diabetic. Wilder separates the arteriosclerotic retinal phenomena from the so-called true diabetic retinitis. In the former the lesions do not appear to be influenced by the severity or degree of control of the diabetes. On the contrary, they appear to be progressive in spite of every form of therapy. Similarly, there appear to be two distinct types of cataract—a true diabetic type said to be reversible by Wilder and the senile cataract. Russell Richardson and his colleagues have published in the *American Journal of Medical Sciences* (1945) the first of a series of studies of 100 patients with diabetes of ten or more

years' duration in one clinic. Subcapsular flocculi occurred in 5 of the 100 cases, and it is stated that the progress of such a cataract can often be arrested by correct treatment of diabetes. Collens and Boas, on the other hand, have not observed the disappearance of this type of cataract, having once developed, no matter how well the diabetes was controlled. It has, in the past, been the practice to ascribe indiscriminately all the misfortunes of the diabetic in the shape of so-called complications, to faulty control of his disease. It must, however, be conceded that certain of these degenerative processes which occur quite commonly in the non-diabetic and deteriorate progressively, are likely to follow a similar course when occurring in the diabetic. Recent investigations are helping to separate those complications which are due to the severity of the disease process and which may be reversible with adequate treatment from those which are not primarily or not entirely due to diabetic factors and which are not influenced by treatment of the diabetes. In the cases we have seen, the incidence of diabetic complications does not appear to have borne any strict relation to the severity of the disease or its degree of control but appears to have arisen in a completely haphazard and fortuitous manner. Genetic factors may be invoked to aid our explanation of the relationship of diabetes to its commonly associated diseases. "That one or more factors may be involved in diabetic heredity is suggested by the high incidence of obesity, of congenital defects especially of mesenchymatous tissue (first reported by Priesel and Wagner), possibly such degenerative lesions as cataract and arteriosclerosis in diabetic patients and the appearance of congenital anomalies, especially of the mesenchymatous tissues in the offspring of diabetic mother." However, there are matters nearer of solution from the standpoint of practical medicine. The hypothesis of a pancreatic hormone stood for many years before Banting and Best provided the proof. We feel that the position is similar to-day in relation to the anterior pituitary gland and that the answer will come from the physiologists and biochemists. Some recent work has carried us further in this belief. Work on the experimental animal will not always bear direct reference to the human subject but an interesting counterpart to the latest experimental work has unexpectedly come to light from studies on pregnant diabetic women. The first suggestion of a possible hormonal imbalance was made by Murphy (1933). He reported that the prolan excretion of two diabetic women exceeded the normal. This work was carried further by Smith and Smith who, estimating hormones in pre-eclamptic toxæmia of pregnancy, quite naturally turned to diabetics as material to study this problem from early to late pregnancy, since the incidence of pre-eclamptic toxæmia in diabetes is more than 30 per cent. These investigators confirmed in diabetics their earlier observation that an excess of serum prolan precedes, predicts and perhaps causes pre-eclamptic toxæmia. White and Hunt subsequently studied this problem in pregnant diabetics.

They confirmed the observation of Smith and Smith and in a large series were able to predict pre-eclamptic foetal accidents by the finding of an abnormally high concentration of gonadotropins in the blood serum after the fifth month of pregnancy. White has carried this work further. On the advice of Smith and Smith a group of patients, whose values for serum prolactin were supernormal, received massive doses of oestrin and, in addition, progestin. In 17 cases so treated the serum gonadotropin level dropped, and 15 of them delivered successfully. It would appear that White has made a significant contribution to the successful management of the pregnant diabetic. It has furthermore been suggested "that since in diabetes hypertension, albuminuria, retinitis and sclerosis occur, and since in our pregnant diabetics one half have demonstrable hormonal imbalance which if untreated is associated with pre-eclamptic toxæmia, and since the long-duration case with the most marked signs of sclerosis has been of an endocrine type, hormone studies should be carried out and substitutional therapy administered if indicated."

Whatever the future may disclose, the facts remain that we are in possession of two effective weapons in our treatment of diabetes mellitus, viz. diet and insulin. Are we making the best possible use of these? We feel that the answer is not an unmodified affirmative. Recent research developments indicate that the static conception of the pancreas in diabetes can no longer be upheld. The evidence points to a continuous struggle between antagonistic factors of which the anterior pituitary factor or factors may prove to be the most important. Insulin counteracts the diabetes-producing factors. How it achieves this we do not know. It would appear possible that diabetes can arise in one of two ways: either the islets of Langerhans are incapable of producing an amount of insulin to meet the requirements of the diabetic organism, or the islets are able to produce sufficient insulin but some other mechanism interferes with its action. Either mechanism may prove to be the correct one or even they may both exist and account for the different clinical types of diabetes. It remains, however, for the physician to make the best use of insulin as far as its activity is understood at present. This requires the close observation and supervision of each individual patient. Each diabetic is a law unto himself. It is agreed that for therapy to be regarded as completely successful, the patient should be allowed to lead a perfectly normal life both from a working and social point of view. If we do not make the diabetic a completely normal and useful member of the community our therapy is not an absolute success. For this reason we advocate that the diabetic should be freed as far as possible from the restrictions that have encompassed him in the past.

We wish to express our thanks to Dr R. W. Brookfield, M.D., Ph.D., F.R.C.P., D.P.H., Honorary Physician, Royal Southern Hospital, Liverpool, for encouraging us to publish this paper and for his criticism.

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## NOTES

At a meeting of the Royal College of Surgeons of Edinburgh, held on 15th December 1948, Mr Frank E. Jardine, President, in the Chair, the following who passed the requisite examinations were admitted Fellows:—Tariq Munir Abbas, M.B., CH.B., UNIV. EDIN. 1943, M.D. 1947; Solomon Abel, M.B., CH.B. UNIV. CAPE TOWN 1938; Angus Fraser Alexander, M.B., CH.B. UNIV. EDIN. 1942; Patrick St George Anderson, M.B., B.CH., B.A.O. UNIV. DUBLIN 1942; Robert William Bailie, M.B., B.CH., B.A.O. QUEEN'S UNIV. BELFAST 1941; John Aulds Barclay, M.B., CH.B. UNIV. GLASG. 1943; Alan Edward Bateman, M.B., CH.B. UNIV. CAPE TOWN 1945; Hugh Alec Benjamin, M.B., B.CH. UNIV. WITWATERSRAND 1945; Constance Lang Beynon, M.B., CH.B. UNIV. EDIN. 1932; Satya Charan Bhattacharyya, M.B. UNIV. CALCUTTA 1934; Hugh Gault Biggart, M.B., B.CH., B.A.O. QUEEN'S UNIV. BELFAST 1942; Hamilton Donald Walter Black, M.B., CH.B. UNIV. NEW ZEAL. 1944; John Stewart Boyd, M.B., B.CH. QUEEN'S UNIV. BELFAST 1941; Ivan Bruce, M.B., CH.B. UNIV. LEEDS 1943; Alexander Buchan, M.B., CH.B. UNIV. ABERDEEN 1936; George Buchanan, L.R.C.P. AND S.EDIN. (TRIPLE) 1940; James Stanislaus Calnan, M.R.C.S. ENG., L.R.C.P. LOND. 1942; James Donald Cameron, M.B., CH.B. UNIV. EDIN. 1934; John Angus Campbell, M.B., CH.B. UNIV. EDIN. 1944; Norman Andrew Campbell, M.B., B.CH. UNIV. CAMB. 1943; John Simmons Cason, M.B., CH.B. UNIV. LEEDS 1942; Zinnur Ahmed Choudhuri, M.B. UNIV. CALC. 1933; Kenneth Scott Clarke, M.D. QUEEN'S UNIV. ONTARIO 1943; Keith Wallace Cochrane, M.B., CH.B. UNIV. NEW ZEAL. 1944; Redmond Brett Gould Cook, M.B., CH.B. UNIV. NEW ZEAL. 1941; John William Cowie, M.B., CH.B. UNIV. EDIN. 1944; Colin Scott Dafoe, M.D., C.M. QUEEN'S UNIV. ONTARIO 1936; Kenneth Hugh Dalrymple, M.B., CH.B. UNIV. L'POOL 1942; William James Dempster, L.R.C.P. AND S. EDIN. (TRIPLE) 1941; William Robert Dickie, M.B., B.CH., QUEEN'S UNIV. BELFAST 1940; Charles Albert Page Donaldson, M.B., CH.B. UNIV. EDIN. 1937; Alan George Gibb, M.B., CH.B. UNIV. ABERDEEN 1941; Colin Allan Gleadhill, M.B., CH.B. UNIV. EDIN. 1939; Archie Gilmour Gray, M.D. UNIV. MANITOBA 1945; Lionel Maurice Green, L.R.C.P. AND S.EDIN. (TRIPLE) 1927; William Swanston Hanna, M.B., B.CH. QUEEN'S UNIV. BELFAST 1942; Phillip Harris, L.R.C.P. AND S.EDIN. (TRIPLE) 1944; Alexander Robinson Harper, M.B., CH.B. UNIV. GLASG. 1938; Cornelius Jeffcott Hassett, M.B., B.CH. UNIV. DUBLIN 1932; Jeruchem Romain Hochhauser, M.D. UNIV. TOULOUSE 1941; Vernon Stanley Hughes-Davies, M.B., CH.B. UNIV. L'POOL 1930; Robert Fred Jackson, M.R.C.S.ENG., L.R.C.P. LOND. 1943; Edwards William Jeyaratnam, L.M.S. CEYLON MED. COLL. 1933; Arthur Joffe, M.B., B.CH. UNIV. WITWATERSRAND 1942; Alexander Macpherson Keith, M.B., CH.B. UNIV. ABERDEEN 1935; John Richard Kenyon, M.B., CH.B. UNIV. GLASG. 1942; David Ronald Kilgour, M.B., CH.B. UNIV. EDIN. 1936; Shreedhar Shreenivas Kirtane, M.B., B.S. UNIV. BOMBAY 1940; Alfred Philip Kitchin, M.B., B.CH. UNIV. CAMB. 1938; John Wallace Knox, M.B., B.S. UNIV. SYDNEY 1943; Tecklim Koonvisal, M.R.C.S.ENG., L.R.C.P. LOND. 1943; Douglas Watson Lamb, M.B., CH.B. UNIV. EDIN. 1944; Archdale Sydney Lewis, M.D., C.M. DALHOUSIE UNIV. CANADA 1943; Robert Alfred Lindsay,

M.B., B.S. UNIV. SYDNEY 1944; Ursula Mary Lister, M.R.C.S.ENG., L.R.C.P. LOND. 1941; Harold Keith Lucas, M.B., CH.B. UNIV. L'POOL 1937; James Theodore Mair, M.R.C.S.ENG., L.R.C.P.LOND. 1936; Rabindra Nath Guha Majumder, M.B. UNIV. CALC. 1933; Thomas Swan Matheson, M.B., CH.B. UNIV. EDIN. 1943; Alistair John Miller Mathieson, M.B., CH.B. UNIV. ST ANDREWS 1942; Abraham Bernard May, M.B., CH.B. UNIV. CAPE TOWN 1935; Ramchand Kishindas Menda, M.B., B.S. UNIV. BOMB. 1938; Isaac Hai Meyer, M.R.C.S.ENG., L.R.C.P.LOND. 1940; Aaron Michel Michael, M.B., CH.B. UNIV. CAPE TOWN 1941; John Phillimore Mitchell, M.R.C.S.ENG., L.R.C.P.LOND. 1942; Robert Morrison, M.B., CH.B. UNIV. EDIN. 1935; John Mowat, M.B., CH.B. UNIV. ABERDEEN 1942; Alastair Allan Murray, M.B., CH.B. UNIV. EDIN. 1936; John Houston McBeath, M.B., CH.B. UNIV. GLASG. 1940; Robert John Murray McCormack, M.B., CH.B. UNIV. EDIN. 1944; Archibald Bruce McCulloch, M.B., CH.B. UNIV. EDIN. 1942; David Moffat Macdonald, L.R.C.P. AND S.EDIN. (TRIPLE) 1937; Gordon Herbert Dargavel McNaught, M.B., CH.B. UNIV. EDIN. 1944; Charles Godfree Nairn, M.B., CH.B. UNIV. GLASG. 1938; John Gordon Napier, M.B., CH.B. UNIV. EDIN. 1940; Edward Lawford Nicolson, M.B., CH.B. UNIV. GLASG. 1934; Thomas Hamlet Norton, M.B., CH.B. UNIV. MANCH. 1938; William David Paterson, M.B., CH.B. UNIV. ST ANDREWS 1945; Bernard Henry Price, M.B., B.CH. UNIV. CANTAB 1938; Ghias-Ud-Din Qazi, M.B., B.S. UNIV. PUNJAB 1946, L.R.C.S.EDIN. 1948; Peter Thomas Quinlan, M.B., CH.B. UNIV. MANCH. 1943; Mohammed Siddique Qureshi, M.B., B.S. UNIV. PUNJAB 1936; Florence Claire Ruth Richardson, M.R.C.S.ENG., L.R.C.P.LOND. 1941; Ernest Francis Ridley, M.B., CH.B. UNIV. ST ANDREWS 1940; Leo Reynolds Robson, M.B., CH.B. UNIV. LEEDS 1935; Peter Ernest Roland, M.R.C.S.ENG., L.R.C.P.LOND. 1939; Norman Rosenzweig, M.B., CH.B. UNIV. CAPE TOWN 1942; Abdel Megid Sadek, M.B., CH.B. UNIV. GLASG. 1943; Himadri Kumar Sarkar, M.B. UNIV. CALC. 1944; Alexander Stewart Scott, M.B., CH.B. UNIV. GLASG. 1936; Lyall Stuart Scott, M.B., CH.B. UNIV. GLASG. 1944; Robert Henry Sewell, M.B., H.B. UNIV. MANCH. 1943; Shrikrishna, M.B., B.S. UNIV. LUCKNOW 1933; Judah Julius Skapinker, M.B., B.CH. UNIV. WITWATERSRAND 1943; Allan Douglas Smit, M.B., CH.B. UNIV. CAPE TOWN 1941; Peter Hugh Eccles Smith, M.B., CH.B. UNIV. BIRM. 1944; Edward Frederick George Stewart, M.R.C.S.ENG., L.R.C.P.LOND. 1938; Blair Alexander Thompson, M.B., CH.B. UNIV. EDIN. 1942; George Russell Thomson, M.B., CH.B. UNIV. GLASG. 1941; Norman Tunnell, M.B., B.S. UNIV. DURHAM 1938; Philip Raby Walbaum, M.B., CH.B. UNIV. EDIN. 1944; Robert Baury Watson, M.B., CH.B. UNIV. CAPE TOWN 1942; Catrin Mary Williams, M.B., B.CH. UNIV. WALES 1945; Robert Guy Williams, M.D. UNIV. ALBERTA 1943; Eileen Dorothy Mary Wilson, M.B., B.S. UNIV. LOND. 1936; David Wright, M.B., CH.B. UNIV. GLASG. 1935; James Hall Wrigley, M.B., CH.B. UNIV. EDIN. 1944; Sidney Zinn, M.B., B.CH. UNIV. WITWATERSRAND 1943.

*Higher Dental Diplomates.*—The following candidates having passed the requisite examinations were admitted Higher Dental Diplomates—Peter Halliburton Burke, L.D.S. UNIV. DURHAM 1942; Henry John Elsey, L.D.S. UNIV. BIRM. 1942; Felix Austin Leslie Fernando, L.D.S. CEYLON 1939, L.D.S., R.C.S.EDIN. 1948; Dorothy Lindsay Deas Johnston, L.D.S., R.C.S.EDIN. 1940; Gilbert James Mills, L.D.S. UNIV. BRISTOL 1941; Geoffrey Emile Moore, L.D.S. UNIV. BIRM. 1944; Herbert David Norton, L.D.S. UNIV. MANCH. 1940; Philip Gordon Rideal, L.D.S., R.C.S.EDIN. 1944.

At a Graduation Cermonial held in the Upper Library on Friday, 17th December 1948, the following degrees were conferred:—

University of  
Edinburgh

*The Degree of Doctor of Medicine*:—James Maxwell Alston, Scotland, M.B., CH.B. (with Second Class Honours), 1924 (*Awarded Medal for Thesis*); William James Matheson, Scotland, M.B., CH.B. 1938; Helen Ronaldson Neve, Scotland, M.B., CH.B. 1929.

*The Degree of Master of Surgery*:—Ewen Alistair Jack, O.B.E., England, M.B., CH.B. 1932 (*Highly Commended for Thesis*).

*The Degree of Doctor of Philosophy*:—*In the Faculty of Medicine*:—Ian Ferguson Sommerville, M.B., CH.B.; Abraham Stolman, B.Sc.(RUTGERS) (*In absentia*).

*The Degrees of Bachelor of Medicine and Bachelor of Surgery*:—Dores Baxter, Scotland; Harold Cameron, Scotland; Isabel Aileen Cossar, Scotland; Jack Darnborough, England; James Christopher Edie, Scotland; William Douglas Elliott, Scotland; Alexander Collier Ferguson, Scotland; Ian Grant Pagan Fraser, Scotland; George Barclay Goodman, Scotland; Alexander Gordon, Scotland; Peter Ford Green, England; Derek Holden Haworth, England; Sidney Peter Addison Henderson, Scotland; John Wilson Herries, Scotland; Colin Francis Hogg, Scotland; John Tunstall Lamb, England; Monty Harold Lawrence, Scotland; Alexander Craigie MacRae, Scotland; Ann Hopewell Miller, Scotland; Mearns Mackenzie Milne, England; Peter Allison Moffat, Scotland; Agnes Connell Doiran Penman, Scotland; Thomas Russell Preston, Scotland; Michael Liam Roden, Scotland; Brian Hastings Shiel, Scotland; Catherine Barbara Grace Sinclair, Scotland; David Morton Wylie Smith, Scotland; Colin Cecil Russell Walker, Scotland; David Cooper Main Wilcox, Scotland.

*Diploma in Tropical Medicine and Hygiene*:—Samuel Rizkalla Abdel Messih, L.R.C.P.(ED.), L.R.C.S.(ED.), L.R.F.P. AND S.(GLASG.)

*Diploma in Medical Radiodiagnosis*:—Leo Darley Keegan, L.R.C.P.(IREL.), L.R.C.S.(IREL.); Lawrence Douglas Philp, M.B., CH.B.; Philip St George Robinson, M.B., B.CH.(DUBL.).

*Diploma in Medical Radiotherapy*:—John Alastair Caskey, M.B., CH.B.; William Bertrand Dawson, M.B., CH.B.; Mary Ann Jeffrey Torrance Douglas, M.B., CH.B.; James Frederic Riley, M.B., CH.B.

*Sister-Tutor Certificate*:—Jeanie Lochhead Braidwood; Margaret MacDonald.

*Certificate in Psychiatric Social Work*:—Bridget Marion Gardiner.

*The Polish School of Medicine at Edinburgh*:—*The Degrees of Bachelor of Medicine and Bachelor of Surgery*:—Jewel Ajzenberg, Bolesław Barczynski, Witold Browarski, Paulina Maria Cieńska, Stefania Cywińska, Jozef Dabrowski, Elżbieta Antonina De Costres, Franciszek Dulian, Franciszek Fundament, Krystyna Maria Gottlieb, Maria Hławiczka, Tessa Holcman, Lucjan Kręcki, Jan Łacny, Krystyna Lourie, Halina Barbara Marszałek, Szabsa Markus, Tadeusz Michał Nowosielski, Roman Starczewski, Eugeniusz Szlamp, Irena Weissman, Antoni Wittek, Ludmiła Zaleska, Bożena Ziolkowska.

## NEW BOOKS

*Practical Anatomy.* Revised and Rewritten by W. E. LE GROS CLARK, M.A., D.SC., F.R.S., F.R.C.S. Pp. xvi+470, with 251 illustrations. London: Edward Arnold & Co. 1946. Price 25s.

The title of this single-volume "dissecting manual" indicates that it is not entirely a new work; and the preface explains that it is based on a book by "six teachers," itself a revised form of the *Practical Anatomy* of Parsons and Wright that appeared over thirty years ago. This new revision has been undertaken on the ground, often mentioned in recent discussion, that the anatomical curriculum "needs to be shorn of a considerable amount of the topographical detail which is still presented to the medical student in current text-books." The preface discusses this proposition; and among the reasons stated in support of it is the plea that it is essential to include in the curriculum other "important aspects of anatomical science" such as "morphogenetic principles," "a thorough grounding in radiological and surface anatomy," "a more systematic study of muscle actions and joint movements," and "an introduction to the principles and methods of experimental anatomy."

This is admirable; but it is a little difficult to see how these things can be attained without previous dissection based on a fuller guide and with fuller description than can be provided in 449 pages for the whole body. It is true that the author gives advice for preliminary study before the dissection of each region and for supplementary study after it. But this would appear to require either that the student should carry into the dissecting room a second book that describes the structures to be examined, or else do most of his anatomical reading away from the "part," which latter proceeding may well tend to foster that "factual memorisation" which Professor Le Gros Clark deplores.

The author agrees that there may be differences of opinion about details that should or should not be included; but it is a little remarkable that in this praiseworthy attempt to reduce the burden on the medical student the index should provide six references to the petrosal nerves—there are even instructions in the text for finding the lesser superficial petrosal "which must be looked for carefully"—and ignore the presence of the median nerve in the upper arm.

This volume is essentially a dissector's guide, and the dissecting instructions flow continuously through the text, interwoven with description. Whether this is the ideal arrangement is again a matter of opinion based on experience of the student's difficulty in dividing his attention between the book and the "part." But, whatever the method of presentation, the amount of anatomical detail that the student must acquire will depend in the long run on his teacher and perhaps on the examination that he has to face.

Under present conditions of "war economy" the book is well produced; and the illustrations, many of them diagrammatic and some capable of improvement, serve their purpose.

*Anatomical Eponyms.* By JESSIE DOBSON, B.A., M.SC. Pp. ix+240. London: Baillière, Tindall & Cox. 1946. Price 30s.

This book is described in the sub-title as "A Biographical Dictionary of those Anatomists whose names have become incorporated into anatomical nomenclature, with definitions of the structures to which their names have been attached and references to the works in which they are described." The introduction contains some interesting comments on the recent tendency to dispense with eponyms; and Professor Wood Jones, in a foreword, deplores a policy that "has deprived the student of his main incentive to learn of the history and of the great masters of the subject."

The loss of some familiar names is certainly to be regretted ; but selection for current use from the mass of eponyms presented here is apparently an insoluble problem. In any case, he would be a poor teacher of anatomy in this country who allowed his students to depend for their knowledge of John Hunter, to take an obvious example, on chance curiosity aroused by " Hunter's Canal."

Although the plan of this book tends to give a very uneven view of the history of anatomy, it is certainly useful to have the sources of eponymous nomenclature recorded for future reference ; but its value would be greater were it not that the detection of obvious errors on points of interest to the Edinburgh Medical School reduces confidence in its general reliability. The account of the " Foramen of Monro " is curiously arranged and contains errors in dates ; neither Sharpey nor Allen Thomson was ever " Professor of Anatomy " in Edinburgh ; nor was D. A. Welsh " Professor of Pathology " here. In some respects the list is almost too complete, but there are some omissions of which the most surprising is " Meckel's Diverticulum."

*Brompton Hospital Reports*, vol. XV. Pp. 192, with numerous illustrations. 1946. Published by the Research Department of the Hospital.

This is another volume of papers published from the Brompton Hospital covering such diverse aspects as carcinoma of the bronchus, spontaneous perforation of the œsophagus, detection of tubercle bacilli by the fluorescent method, the segments of the lungs and their clinical recognition and the benefits derived from such knowledge. Other authors contribute the results of their work on clinical problems investigated while serving with African troops. Interspersed with these clinical articles one is glad to find some equally good historical essays.

A collection of excellent papers of practical value and well illustrated.

*Child Health and Development* : A Symposium by Specialist Contributors. Edited by R. W. B. ELLIS, O.B.E., M.D., F.R.C.P. Pp. 363, with 49 illustrations. London : J. & A. Churchill Ltd. 1947. Price 18s.

This book is divided into two sections, the first dealing with the physical, emotional and intellectual development of the normal child, whilst in the second are described the various social services related to child health. The first section is well arranged but the content is variable, some chapters, notably that on growth, being exceptionally good ; but the standard of certain other chapters is decidedly mediocre, which is surprising in a symposium by specialist contributors. This first section is too advanced for nurses and social workers, and it is doubtful whether it has a place as a contribution to medical education. The second section is interesting and will be illuminating to many in revealing the number of bodies and ministries concerned with the problem. The book is intended for all those interested in child health from the doctor to the social service worker : it is doubtful whether it will be particularly helpful to either group, though a book for each rather more complete than the two sections comprising this one, might serve a useful purpose.

*Medicine*. Vol. I. By A. E. CLARK-KENNEDY, M.D., F.R.C.P. Pp. xii+383. Edinburgh : E. & S. Livingstone Ltd. 1947. Price 20s. net.

This volume deals with the patient and his disease. A second will be devoted to diagnosis, prognosis and treatment. Impressed by the progressive accumulation of knowledge contained in the current text-books, whereby the memory is strained to breaking point and principles are crowded out or buried under the sheer weight of accumulated facts, the author has applied himself to correlating the many branches of medicine. His purpose has been to indicate the general principles underlying medicine as a whole, to inculcate an attitude of mind which will make the reader think and to create a framework on which a knowledge of medicine can be built by self education as experience widens. This is what he believes is an urgent need. An unusual or novel approach is always intriguing. The present work, in which the

author, *inter alia*, gives due weight to the personal or humanistic side of medicine, will appeal to, stimulate and widen the outlook of the intelligent practitioner.

*Mongolism and Cretinism.* By CLEMENS E. BENDA, M.D. Pp. 330, with 101 illustrations. London: William Heinemann (Medical Books) Ltd. 1947. Price 25s. net.

Every medical student spends a certain amount of time learning how to differentiate a cretin from a mongol, and, having done this, dismisses the latter as an exhaustion product but may, and often does, further his inquiries about cretins, probably because many eminent investigators of the past have studied the cretin in detail. The author of *Mongolism and Cretinism* has done much to redress this discrepancy, and presents a very comprehensive and clear picture of Mongolism, or, as he prefers to term it, acromicria—in contrast to acromegaly—as he understands the condition. The subject matter is very well presented and stimulates a deal of interest on aspects which have not received attention in the past; the illustrations are excellent. As well as to those especially interested in mental deficiency, this book will be greatly welcomed by everyone interested in pædiatrics, obstetrics and endocrinology, but it will be a pity if it does not reach a much wider field in the medical profession for it is a real contribution to medical literature.

*Handbook of Elementary Anatomy.* By J. J. TEKLENBURG. Pp. 16. London: H. K. Lewis & Co. Ltd. 1947. Price 5s. 6d. net.

This small book is an atlas of 16 plates illustrating human anatomy. Some of the pictures are very diagrammatic, others are fairly realistic. All are numbered in such a way that each item can be readily identified. There is no descriptive matter. The book is primarily intended for nurses and first-aid students and should prove useful.

*1947 Year Book of Orthopædic and Traumatic Surgery.* Edited by EDWARD L. COMPERE, M.D. Pp. 438, with 256 illustrations. Chicago: The Year Book Publishers. 1948. Price \$3.75.

This annual appeared formerly under the title *Year Book of Industrial and Orthopædic Surgery*. The title was changed because it was felt that most of the material in the current literature on industrial surgery could be more correctly classified as orthopædic or traumatic surgery. Traumatic surgery is considered only as it is applied to the locomotor system. The present volume follows the plan of former volumes. Extracts are taken from the world literature and in many cases short critical comments are made by the editor. Sub-sections deal with either general conditions, such as tumours and arthritis, or special regions, such as shoulder, feet, etc. The reproduction of illustrations is very good.

The book can be strongly recommended. It should be in possession of all orthopædists and those who deal with traumatic cases.

*New Ways of Treating Uremia.* By W. J. KOLFF, M.D. Pp. 112, with 53 illustrations. London: J. & A. Churchill Ltd. 1947. Price 10s. 6d.

The artificial kidney, peritoneal lavage, perfusion of an isolated intestinal loop, and high caloric low protein diets, are the four measures discussed. Very full details of all the treatments, except the last, are given. Scale plans and excellent illustrations add to the wealth of detail provided.

The successful use of the artificial kidney and peritoneal lavage appears at present to be limited to selected cases of uræmia arising acutely. It is proposed to employ the former "as soon as" the blood urea exceeds 350 mgm. per cent. and "before that if moreover" the potassium content is raised or the alkali reserve is too low. The rate of urea clearance obtained with peritoneal lavage is 15 c.c. per minute, with the artificial kidney it is more than 100 c.c. per minute.

The scant description of the dietetic treatment contrasts unfavourably with the rest of the book.

## NEW EDITIONS

*Kompendium der topischen Gehirn und Rückenmarksdiagnostik.* By R. BING.  
Thirteenth Revised Edition. Pp. 288, with 130 illustrations and 3 tables.  
Basel: Benno Schwabe & Co. Price 25 Swiss francs.

The newest edition of this popular book by the Nestor of Continental Neurology follows the last one after only three years.

Relevant experience from injuries to brain and spinal cord during the last war have been partly incorporated. Recent advances in clinical neurology and pathology and the revived international intercourse have benefited the book. Professor Krayenbuehl, Director of the Zürich University Neuro-Surgical Klinik, contributes an arteriogram and suggested the brief survey of topical diagnosis of congenital aneurysms, a lesion, according to Bing, still largely unknown to physicians in spite of its relative frequency.

As a whole, the book remains what it was since it first appeared in 1909; a sober, didactic registration of the diagnostically useful, based on sound clinical observation. The illustrations and tables have been reproduced by many textbooks the world over.

Indispensable to a generation without mechanical helps to localisation, it can still be warmly recommended, even though a revision in the light of twenty-five years of research; anatomical, physiological, experimental and neuro-surgical, would perhaps make a stronger appeal to English-speaking readers.

*Diseases of the Nose, Throat and Ear.* By W. L. BALLENGER, M.D., F.A.C.S., H. C. BALLENGER, M.D., F.A.C.S., and J. J. BALLENGER, B.S., M.D. Ninth Edition. Pp. 993, with 16 plates and 597 figures. London: Henry Kimpton. 1947. Price 63s.

This is a large and complete textbook of the subject from an author whose name is a household word in the specialty, and its popularity is evidenced by the fact that it has reached the ninth edition.

The book is produced in first class style. The paper and printing are good and it is profusely illustrated with diagrams and illustrations which are on the whole of an excellent standard.

In subject matter the book is surprisingly uneven for a ninth edition, and there are some inaccuracies which may be due to the authors' unwillingness to commit themselves definitely on certain points. We wonder what evidence the authors have that strychnine is of value in the treatment of bilateral abductor paralysis, or galvanism in the treatment of angioneurotic deafness. Surely in a textbook of this class such doubtful therapeutic measures could be omitted. Sinusitis and its complications is well done, but there is a regrettable lack of mention of the effects of ear disease upon the function of hearing, and the measures to combat it.

There is a new chapter on headaches which is to be commended as a laudable attempt to give some light on a most troublesome subject.

The style is readable if uninspiring, and for those who wish a single book on this subject this is probably the best there is.

*Index of Modern Remedies.* By WILLIAM MAIR, F.R.S.E., F.C.S., M.P.S. Fourth Series. Pp. 68. Glasgow: "The Scottish Chemist." 1948. Price 3s.

Mr Mair is again to be congratulated on bringing out an up-to-date version of his most useful booklet. Recent preparations are so numerous that no one could be familiar with the composition and actions of all of them, or even with their names—hence the value of such a compilation as this.

In format and content the present edition resembles the previous ones but it contains a great deal more. There is also a summary of the changes introduced by the new British Pharmacopœia.

This book is indispensable to all who wish to keep abreast of the times.

*Handbook of First Aid and Bandaging.* By A. D. BELILIOS, M.B., B.S., D.P.H., D. K. MULVANEY, M.S., F.R.C.S., F.R.C.P., and K. F. ARMSTRONG, S.R.N., S.C.N., Third Edition. Pp. xii+512, with 245 illustrations. London: Baillière, Tindall & Cox. 1948. Price 5s. net.

This book is one of the most up-to-date and practical handbooks on first aid and bandaging that has been written. The text is clear and concise and is illustrated with excellent diagrams. The chapter on chemical warfare has been deleted while sections on hæmorrhage, spinal injuries, heat exhaustion and heat stroke have been included. This book will prove of great value to all lecturers in first aid, first aid workers and nurses.

*Handbook of Practical Bacteriology.* By T. J. MACKIE, C.B.E., M.D., D.P.H., and J. E. MCCARTNEY, M.D., D.SC. Eighth Edition. Pp. viii+624. Edinburgh: E. & S. Livingstone Ltd. 1948. Price 25s. net.

The eighth edition of this book keeps up the high standard of its predecessors. The book has been completely revised and all recent developments in bacteriological knowledge and technique have been included in the text.

It can be highly recommended to all those engaged in bacteriological work and study as a concise yet full textbook of the subject.

*The Science and Practice of Surgery.* By W. H. C. ROMANIS, M.A., M.CH., F.R.C.S., F.R.S. (EDIN.), and PHILIP H. MITCHINER, C.B., C.B.E., T.D., M.D., M.S., F.R.C.S., D.CH. Eighth Edition. Volume I, pp. vi+892, with 479 illustrations (or 20 plates and 409 illustrations). Volume II, pp. viii+955, with 345 illustrations (or 8 plates and 316 illustrations). London: J. & A. Churchill Ltd. 1948. Price 25s. each volume.

Most readers will be pleased to find that the authors of this well-known textbook have resisted suggestions that it should be made more simple and more dogmatic. The detailed accounts of clinical conditions and the descriptions of alternative methods of treatment have always been distinctive and valuable features of the work.

All the sections have been thoroughly revised for this edition, and valuable new chapters of the principles of plastic surgery and radiotherapy have been added. Considerable alteration has been made to give adequate place to chemotherapy and the antibiotics, but it is disappointing to find that the surgery advised to supplement the penicillin treatment of acute osteomyelitis is open drainage. Another minor criticism is that too many of the older illustrations depict gross lesions of an advanced type which medical students are not likely to see now. These may demonstrate awful possibilities, but are not helpful in teaching diagnosis. The illustration of "sound leg traction" for fractured neck of femur (ascribed in the text to the Edinburgh School) is a sad travesty of the butterfly splint.

In spite of such minor faults, this new edition is to be welcomed as a very adequate revision of a deservedly popular work.

*Cardiovascular Diseases: Their Diagnosis and Treatment.* By DAVID SCHIFF and LINN J. BOYD. Second Edition. Pp. xii+743, with 56 illustrations. London: William Heinemann (Medical Books) Ltd. 1948. Price 63s. net.

The first edition of this book appeared in 1939 and was translated into seven languages. In producing the second edition, the authors have re-written the book



completely. Instead of a series of essays on selected subjects, there is now offered a detailed discussion of cardio-vascular diseases in their many aspects. The result is a book of first-rate value to all interested in the subject.

The book opens with six valuable chapters on general subjects, *e.g.* Dyspnœa, Hypertrophy and Dilatation, Compensation and Decompensation, and goes on with chapters on the conventional anatomical and pathological groupings, including one on Rheumatic Fever. There is a most useful section of 72 pages on Peripheral Vascular Diseases and a separate chapter is devoted to Therapy. An extensive bibliography of world literature is provided after each chapter.

The reviewer finds surprising the absence of any discussion of modern ideas on high- and low-output failure, on the action of digitalis, and on the value of the cardiac catheter in the investigation of congenital cardiac defects.

The book is characterised by solid and critical commonsense, freedom from extravagance, and a lucid readable style, and can be recommended with complete confidence.

*The Practice of Local Anæsthesia.* By GEORGE BANKOFF, M.D., D.CH., F.R.F.P.S.G., F.R.C.S.E. Third Edition. Pp. 290, with 199 illustrations. London: Staples Press Ltd. 1948. Price 30s. net.

This volume falls between being a short practice of the essential techniques of local analgesia and a more complete textbook. An attempt has been made to cover the whole subject, but some items might well have been omitted because of inadequate treatment: for example, the table of contents includes "blocking of the stellate ganglion" which is dismissed by a generalisation in six lines of no practical value. The chapter on Auxiliary Methods of Local Anæsthesia is not up to date, shows some irrelevancy, redundancy, lack of exactitude and a failure to appreciate certain practical points of importance. It is inconsistent to state that failure to induce anæsthesia with barbiturates is due to "inadequate disintegration" of the drug and to offer the same explanation for prolonged unconsciousness following its use. In the same chapter the author has left uncorrected a misleading error in respect to the dosage of pentothal which was pointed out in a review of an earlier edition.

Most of the sections have good practical detail and the illustrations throughout are excellent, although in respect to the latter, it would have been helpful to the reader if the author had referred to them in the text by their numbers which are otherwise of little use.

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|---|-----------|
| BRODAL, A. Neurological Anatomy in Relation to Clinical Medicine.<br>(Oxford University Press, London)  | 42s. net. |
| GABRIEL, WILLIAM B., M.S.LOND, N.R.C.S.ENG. The Principles and Practice.<br>of Rectal Surgery. Fourth Edition. (H. K. Lewis & Co. Ltd., London) | 16s. net. |
| ISRAELS, M. C. G., M.SC., M.D., M.R.C.P. An Atlas of Bone-Marrow Pathology.<br>(William Heinemann Medical Books Ltd., London)                   | 30s. net. |
| MAINGOT, RODNEY, F.R.C.S.ENG. Abdominal Operations. Second Edition.<br>(H. K. Lewis & Co. Ltd., London)   | 84s. net. |
| Edited by MASSEY, ARTHUR, C.B.E., M.D., D.P.H., D.P.A. Modern Trends in<br>Public Health . . . . . (Butterworth & Co. Ltd., London)             | 50s. net. |
| MONRAD-KROHN, G. H., M.D., F.R.C.P. The Clinical Examination of the<br>Nervous System. Ninth Edition. (H. K. Lewis & Co. Ltd., London)          | 16s. net. |
| TORPIN, RICHARD, M.B. A Treatise on Obstetric Labor.<br>(Augusta Obst. & Gyn. Book Co., Augusta, Ga. U.S.A.)                                    | \$7.00    |

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